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THE HERNIATED INTERVERTEBRAL DISK*

An Analysis of 400 Verified Cases

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IN THE last ten years considerable material has appeared in publications indicating that the presence of herniated intervertebral disks is not a myth but a proved entity, producing a train of symptoms and signs that are as characteristic as are those of renal colic or appendicitis. As is so true of all new developments, there are always those who are overenthusiastic in the treatment of this disease and those who are skeptical about it.

It is astounding to find that so many proved ruptured disks have been discovered in such a comparatively short time. Inasmuch as it is known that this condition was present since man first assumed the upright position, and that many patients with the now characteristic group of symptoms of a herniated disk did quite well on conservative measures, one must wonder whether or not much of the surgical interference that is now instituted may not be superfluous or even unjustifiable. It is with this in mind that 400 operatively proved cases, in which eighteen months to ten years have elapsed since surgical intervention, have been studied.

An interpretation of one's results cannot be entirely unbiased, and what one surgeon would consider a good result may be judged a poor result by another. All factors must be weighed carefully, such as the personal factor, — the surgeon, industrial surgeon and employee, — the discomfort and disability of the patient before operation as compared with his postoperative symptoms, the ability of the patient to carry out his usual occupation, and his wage-earning capacity. This survey was made on the assumption that most patients are honest, and therefore considerable reliance was placed on the patient's statements whether they considered the results satisfactory. If, however, a patient thought that the result was satisfactory but the facts indicated that he was not back at his usual occupation because doing so resulted in considerable low-back discomfort and necessitated frequent absence from work, this result was certainly not satisfactory from the industrial surgeon's or employer's standpoint. The patients were checked personally, but they were also requested to answer a questionnaire that gave additional information. In this manner it could be determined with reasonable accuracy whether the operative procedures instituted were justifiable in each case.

There can no longer be any skepticism concerning the presence of the herniated disk and its actual participation in the production of low-back pain and sciatica. There is, however, no question that the time and type of treatment to be instituted are still somewhat vague. For this reason one must not be too decided in his opinion about the proper treatment in a given case until a thorough history has been taken and a complete physical examination, including a bone and joint as well as a neurologic survey, has been made. The laboratory studies should include the usual blood and urine examinations, and roentgenograms of the lower spine and sacrum should be made. These studies usually rule out the more frequent causes of low-back pain with sciatica, such as osteoarthritis, metastatic malignant bone lesions, angiomas of the bone, osteomyelitis, old compressed fractures, Marie Strümpell arthritis, diabetic neuritis, syphilis, and postherpetic neuralgia — evidenced by segmental scars on the skin.

Spinograms should not be used in every case. Certainly, if all the studies have been normal, in the presence of a typical history of a herniated disk as well as typical neurologic findings, it is usually safe to carry out an exploratory operation. Roentgenograms with a contrast medium (oxygen is used exclusively at the Lahey Clinic) should emphatically be made, however, in the following four types of case. The first group comprises patients who have severe sciatica that has not responded to conservative measures in three weeks. If a large defect is present, an exploratory operation is indicated. If a small or no defect is present, one may justifiably continue conservative measures. The second group includes those in whom either the history or the

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findings are atypical. The third group is comprised of patients with low-back pain in whom a fusion is contemplated, unless exploration is to be carried out at the time of fusion. The fourth group is formed of patients in whom roentgenograms of the lumbar spine show marked degenerating changes with spur formation.

The study of the 400 cases was instructive because of the fact that the histories were uniformly characteristic. The physical findings varied considerably, depending entirely on the time the patient was examined and whether the condition was in an acute, subsiding or quiescent state. During the quiescent stage the findings in many cases were absolutely normal. Since, therefore, the patients were examined in varying stages, the percentages quoted in the findings must necessarily be different than would be the case if every patient had been examined only during the acute stage.

Clinical Data

Frequency

This series represents 8 per cent of the patients who entered the clinic with the outstanding complaint of low-back pain, with or without sciatica. This emphasizes the point that even though the herniated disk is an important link in the chain of conditions that cause low-back pain and sciatica, it is by no means the predominant one.

Etiology

It is of interest that 7 patients belonged to families several members of which had had herniated disks. In one family there were two sisters and one brother; in another, two brothers and sisters. A history of injury was given in 65 per cent of the cases. It is significant that the usual account of injury was that of a sudden lifting strain during which the patient felt a snap in the low back and immediately experienced either a numbness and tingling in one leg or a sudden, severe, sharp pain. In many cases, however, the paresthesia or pain did not come on until several hours or days later. It is somewhat difficult to explain why ruptured cartilages do not follow severe injuries such as compression fractures or dislocated fractures of the spine. It appears that actual rupture may take place into the crushed bodies rather than posteriorly, and that during the period of convalescence actual bony union takes place, incorporating the injured disk, and in that manner prevents later herniation.

There can be little question that rupture of disks occurs most frequently at the site of greatest mechanical stress and strain in both the cervical and lumbar regions. The fact that 68 per cent of the cases occurred in males and 32 per cent in females also tends to favor trauma, especially since 84 per cent of the cases occurred in patients between the ages of twenty and fifty and about equally divided in these three decades. Sixty-five per cent were manual laborers and 35 per cent professional workers. In only 6 per cent of the patients were there demonstrable anomalies, such as spina bifida occulta. Abnormally placed facets were frequent.

Subjective Symptoms

The duration of symptoms varied greatly. There was no accurate way of determining the actual time element, since in all the cases the symptoms tended to occur periodically, lasting from a few days to several months and occurring over a period of up to twenty years.

Recurrent low-back pain was present in 95 per cent of the patients. It preceded the sciatica in many cases and appeared simultaneously with the leg pain in the remainder, in some cases being located one or two vertebras higher than the herniated disk. Sciatica was present in every case except 2, in which there was severe mid-low-back pain, coming on at intervals. Both patients proved to have midline ruptures without compression on separate nerve roots.

In 63 per cent of the patients the sciatica was unilateral. It must be emphasized that the pain must be in the sciatic distribution if the disk is at the fourth or fifth lumbar segment, and any pain that is not limited to it must be viewed with skepticism in the diagnosis of herniated disk. Nine patients had pain in the thigh due to herniated disks at the second or third lumbar segment. The exceptions to the rule hold true, however, and in this series 5 patients had associated severe pain in the inguinal region. Seventy-five per cent of the patients complained of pressure paresthesia. Minor motor changes were noted in many cases. Paralysis, however, was the chief complaint of 6 patients. Fifty-two per cent of the patients complained of radiating pain into the leg on coughing or sneezing. Constipation was present in 47 per cent of the series, probably because straining at stool accentuated the leg discomfort. The fact that patients with herniated disks are usually more comfortable while lying down is important to remember, in contradistinction to those with cauda equina tumor, in whom pain is usually less in the upright position.

Objective Findings

The most constant objective finding was a positive straight-leg reaction, which was present in 90 per cent of the patients when the protrusion was at the third, fourth or fifth lumbar segment. It is safe to say that this test would be positive in nearly 100 per cent of patients if they were examined during an acute phase of the condition. Certainly, if a patient is in a supposedly acute phase and a positive straight-leg reaction is not present, other pathologic factors should be suspected.

Seventy-five per cent of the patients demonstrated definite spasm of the low-back muscles. Localized paraspinous tenderness was present in

80 per cent. Forty-eight per cent had sensory changes in the fifth lumbar or first sacral dermatomes or both. In 35 per cent, list of the spine occurred away from the site of the lesion. In 45 per cent, atrophy of muscle groups — gluteal or calf — or of the extremity from disuse was noted. Fibrillary twitchings were present in 25 per cent. An absent Achilles reflex was noted in 43 per cent, being most frequent with herniated disks at the fifth lumbar segment.

The spinal-fluid studies showed an elevated total protein in only 53 per cent of the patients. Evidence of spinal-fluid block was found in only 2 per cent of the cases. This may be accounted for partly by the fact that in the early group the lumbar puncture was always made in the fifth lumbar space, whereas it is now usually made in the third lumbar space.

Roentgenograms of the lumbosacral spine demonstrated a narrowed interspace at the site of the disk in 15 per cent of the series, localized arthritis (possibly traumatic) in 20 per cent, and an unstable lumbosacral joint in 11 per cent. No characteristic finding indicating a herniated disk was noted in the routine roentgenograms of the spine. Narrowing of the disk space was not an assurance that a posterior dislocation of a disk was present. From these experiences, a normal roentgenogram of the low spine in the presence of a typical history and findings is an additional indication of the probable presence of a ruptured cartilage.

Potentially unstable lumbosacral joints — abnormally placed facets — were present in 6 per cent of the cases. Congenital defects, such as spina bifida, occurred in 6 per cent, indicating at least that congenital malformation demonstrable roentgenologically was not an important factor in producing ruptured cartilages.

Treatment

The best treatment of herniated disks will remain a subject of debate for some years to come. Conservative surgeons will continue to treat patients much along the same lines as they have treated them in the past — by physiotherapy, immobilization, traction, epidural injections, manipulations and so on. The enthusiasts will, of course, operate on all patients who have symptoms. There are also those who will try to maintain a middle course, attempting to determine which patient should be treated conservatively, which should have simple removal of the disk, and which require a combined removal of the ruptured cartilage and fusion. It is the latter course that would be ideal. The only disadvantage about this position is that with the present knowledge there is no definite rule by which the proper treatment in each case can be determined, and there will not be until at least ten to fifteen years have elapsed so that the results of treatment can be adequately compared. Sufficient time has elapsed and an adequate number of patients have been treated, however, so that at least certain facts can be kept in mind when the decision concerning treatment is considered.

There is no question that operative procedures were instituted in some cases reported in this series in which conservative measures would have adequately taken care of the situation, but in no case was the condition made worse, except temporarily by postoperative discomfort. Certainly, one should consider the tolerance for pain and the disability of each patient, to decide whether the situation in all its details and findings is typical or atypical, and to make use of these interpretations in deciding on the form of treatment.

Any patient who has had repeated disabling attacks of sciatica necessitating narcotics and who in the previous few months has been unable to work because of a ruptured cartilage should, in my judgment, have operation. When a patient has had mild recurrences of symptoms causing considerable discomfort but not severe enough to discontinue work at any time, he should just as certainly, in my opinion, be treated conservatively. In the latter case, if the neurologic examination shows considerable evidence of root compression, even though the pain is not severe, the patient should have the benefit of surgery.

In any patient who has been disabled with severe pain only for one or two days out of the year, and between attacks is normal, conservative treatment is justified. By conservative measures is meant physiotherapy in the form of heat, massage and postural exercises, rest in bed on a firm mattress and administration of large doses of Betaxin intravenously for a few days. Betaxin is given in an attempt to relieve the associated mechanical radiculitis. Infiltration with procaine locally into the muscle is also of value.

When operation seems indicated, the question naturally arises whether fusion should be carried out at the time the disk is removed. It seems logical that any patient with predominating leg pain (sciatica) and with minor back difficulty whose roentgenograms show no bone changes should have only the disk removed if this is done through a small exposure, whereas in a patient who has predominating back pain, with definitely abnormal facets and evidence of an unstable back, and who has to do hard manual labor, removal of the degenerated cartilage with fusion is indicated. With the latter state, the long initial hospital stay and inability to work may finally prove to be a shorter course in obtaining relief than would have been the case if the disk alone had been removed.

Adequate removal of all the degenerated cartilage should be done in all patients operated on for herniated disk. It is not sufficient to remove only the loose, fragmented portions.

Postoperative Course

The immediate postoperative course of the patient operated on for a herniated disk is usually smooth, the patient being allowed any liberty he wishes to take. There is no objection to having him stand beside the bed to urinate any time after he has recovered from the anesthetic agent. The back rest is adjusted to any position in which the patient is most comfortable. He is usually up on the seventh postoperative day. The time of getting out of bed after an operation for herniated disk is best left in some degree to the judgment of the patient. Some patients have considerably more discomfort than others and for varying lengths of time after operation. The most annoying postoperative symptoms that occurred in this series were severe spasms of pain in the low back, involving the muscles of the thighs as well. These spasms frequently come on at night, lasting for several minutes and occurring three or four times during the night. They are controlled only by fairly large doses of narcotics. These pains usually occur on the fourth to the seventh postoperative day and last for several days. In 1 case they lasted for several weeks. The incision was reopened in 2 of 10 cases in which these spasms of pain occurred, but nothing was found to account for them except local postoperative swelling of tissue.

Infection occurred in 3 patients. Opening the incision widely and allowing adequate drainage as soon as the infection was noted, with liberal use of the sulfonamide drugs, brought about wound healing in a few days.

The shortest postoperative stay in the hospital was four days and the longest five weeks; the average stay was twelve days.

Late Results

The late results are analyzed in Table 1.

The relief of sciatica was satisfactory in most of the cases. Residual back discomfort on heavy lifting or sitting in a cramped position for many hours occurred in almost half the patients. This percentage was not materially altered in those who had also had fusions, who comprised 9 per cent of the series. It must be admitted that of the patients in whom fusion was performed the predominant symptom was low-back pain, even though associated with sciatica, and that the roentgenograms showed unstable facets with localized reaction at the level of the ruptured cartilage. Two patients complained of severe occurrences of low-back pain in whom spinograms demonstrated midline protrusions at the fourth lumbar space that were verified by exploration. Even though only low-back pain was complained of with no associated sciatica, simple removal of the ruptured cartilage was performed. One patient was completely relieved; the other has had no further severe pain necessitating bed rest, but has been unable to carry on his usual work in a foundry because of low-back discomfort.

TABLE 1. *Analysis of Late Results.*

LATE RESULT	PERCENTAGE OF SERIES
Relief of pain:	
Complete relief of pain	65
Complete reduction in sciatica	90
Reduction in symptoms:	
75 to 90 per cent	20
50 to 75 per cent	10
No relief	5
Return to usual activity:	
Returned in 1 to 3 months	30
Returned in 3 to 6 months	30
Returned in 6 to 12 months	35
No return	5
Unable to do heavy lifting without low-back discomfort	60
Able to do everything without discomfort	38
Complaint of low-back discomfort when tired	40

The ability to return to work in their usual capacity is encouraging to these patients. This ability depends to some degree on the information that the patient is given before the operation. It must be made clear to him that just because he has had an operation on his back does not mean that it has been weakened and therefore he must be careful of it. Co-operation between the employer, surgeon and patient is highly important. It seems unwise to ask the patient to do a full day's work the day he reports for duty. One must keep in mind that these patients have not used the muscles that are ordinarily exercised in their work and therefore have to be gradually conditioned, just as in any athletic sport in which different groups of unconditioned muscles must be built up gradually. Permanent damage, both physical and mental, can be done by unintelligent conditioning by either the patient or the employer. For this reason postural exercises and physiotherapy are extremely important parts of the postoperative care.

In 15 per cent of the series the patients did not obtain relief; in the majority of cases this was not the result of recurrence. All patients who have persistent leg pain, however, must be suspected of having either a recurrence in the same space or another disk rupture above or below the space where the ruptured cartilage was removed, or a persistent radiculitis. In a few patients posterior spur formation — so-called "eagle-beaking" — of bone from localized degenerative changes takes place, and if the nerve is not adequately decompressed, persistent leg pain will remain.

COMPLICATIONS

In discussion of this subject emphasis has been placed on the complications that may result from surgery. In competent hands, however, no serious sequelae should follow operation. There were no deaths or paralysis in any of the patients operated on in this series, even though in several cases a root segment was intentionally sacrificed in an attempt to relieve pain. In 1 case injury was unintentional. There were no demonstrable alterations

except slight sensory changes in the lateral aspect of the foot and inability to spread the small toes.

It is important to emphasize what may happen if a patient who has a large ruptured cartilage remains untreated or is treated by nonsurgical methods. In replying to patients who inquired what would happen if operation was not undertaken, it was my original policy to say that so far as I knew, nothing would happen except that the periodic attacks of pain and incapacitation for work would persist for varying periods of time; that, after all, herniated disks had been present for many years in many cases, even though unrecognized except when causing paralysis; and that the present method of proving their presence and taking care of them had been in use only in the last decade. This advice and the logic back of it were unjustifiable, as indicated by the fact that in 6 cases in this series sudden complete paraplegia developed as a result of ruptured cartilage. Of these patients, 2 who had previously always been relieved by careful manipulation by competent osteopaths developed the paraplegia immediately following manipulation; 2 were manipulated by highly competent bone and joint surgeons and were paralyzed when they awakened from the anesthesia; 1 made a sudden misstep and developed an immediate cauda equina-paralysis syndrome; and 1 gradually developed a cauda equina-tumor syndrome with complete paralysis. In the last case, operation revealed a large disk with an associated adhesive arachnoiditis that completely obliterated the lumbar canal. Even though the protruded cartilages were removed in a relatively short time following the paralysis, many weeks and months elapsed before complete function returned. In 2 of these 6 patients five years after removal of the herniated disk, there is still a marked residual that prevents normal activity.

SUMMARY*

Four hundred proved cases of ruptured intervertebral disk in one or more spaces have been analyzed on the basis of objective and subjective symptoms, and the results eighteen months to ten years after operation have been presented. Hence, no reference to the literature has been made.

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*This article comprises an analysis of a series of cases seen in a single clinic over the course of ten years and comparative opinions concerning diagnosis and treatment have purposely not been discussed.

CARDIAC FAILURE ASSOCIATED WITH ACUTE ANEMIA

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IT HAS long been known that anemia has a profound effect on the heart. In 1857, Bamberger[1] pointed out that cardiac enlargement was found in many patients suffering from chronic anemia, a finding that has since been confirmed by many observers. In 1931, Ball,[2] for the first time, demonstrated such enlargement by x-ray and showed that the diameter of the heart returned to within normal limits after the anemia had improved. This finding also has been confirmed by other investigators.[3, 4] In 1939, Ellis and Faulkner[5] studied the hearts of 64 patients suffering from anemia. Of 38 cases examined by x-ray, 20 showed cardiac enlargement, and of 26 that were followed, 18 showed a decrease in the heart size with improvement of the hemoglobin level. It was also found that the anemia tended to produce a lowering of the systolic and diastolic blood pressures. Electrocardiographic studies were carried out. Of 29 patients who were followed, 7 showed abnormal records; in 5 cases these became normal as the blood level increased. With one exception the abnormal records were consistent in that a depression of the ST segment and a flattening or inversion of the T waves in Lead 1 or in Leads 1 and 2 was present. Of the 47 patients studied, 35 suffered from dyspnea, which disappeared in the cases in which the anemia improved. Twenty-one patients showed dependent edema, and in 10 of the 12 patients with edema who were followed, the edema disappeared with the anemia.

Because of the comparative rapidity with which the heart decreases in size once the anemia is relieved, it is generally believed that its enlargement is mainly due to dilatation. Cabot and Richardson,[6] however, found from autopsy material that there was an increase in the weight of the heart in 18 of 19 patients dying of pernicious anemia, and Porter[7] observed a heart weighing 630 gm. in a man dying of hookworm anemia. These findings have been confirmed by animal experimentation. In addition to dilatation and hypertrophy, the heart muscle undergoes fatty degeneration, which is usually most marked in the papillary muscles of the left ventricle, where it produces a speckled appearance under the endocardium, to which the descriptive phrases "tabby cat," "thrush breast" and "tigering" have been applied. These changes in the myocardium have been produced experimentally by Campbell[8] by subjecting animals to low oxygen pressures for long periods. Also, Opitz[9] in 1935 described areas of myocardial necrosis in patients suffering from severe anemia, and Buchner and

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von Lucadou[10] demonstrated electrocardiographic changes and areas of myocardial necrosis in animals in which severe anemia had been produced.

It will be noted that in every case described above the anemia was chronic, and that although these cases serve to show clinical and anatomic evidence of cardial involvement in long-standing anemia, no mention is made of acute anemia. The cases included in the present report, on the other hand, are associated with acute anemia following massive hemorrhage. Interest was aroused in this group by encountering a few cases at the autopsy table in which cardiac infarction was found in association with hemorrhage from some point in the gastrointestinal tract. Review of the literature reveals that scant attention has been paid to lesions of the heart following acute hemorrhage. In 1937, Bean,[11] reporting a study based on 300 autopsied cases of myocardial infarction from the material of this laboratory, mentioned 2 cases in which the onset of symptoms followed massive hemorrhage. In 1940, McLaughlin, Baker and Sharpe[12] reported the case of a fifty-nine-year-old man who developed a myocardial infarct following massive hemorrhage from a duodenal ulcer. In 1940, Master and Jaffe[13] described the case of a nineteen-year-old girl who suffered from severe ulcerative colitis with frequent severe hemorrhages. The hemoglobin was 19 per cent and the red-cell count 1,000,000. The electrocardiogram revealed depression of the RST segment and low T waves in the three standard leads and in the chest lead — findings that were interpreted as indicating myocardial damage. At autopsy there was infarction of the anterior and posterior papillary muscles, although the coronary arteries were not affected. These writers stated that changes may appear in the electrocardiogram if the hemoglobin falls below 25 per cent. In 1942, Boas[14] described the case of a fifty-five-year-old man who suffered from typical angina pectoris. The electrocardiogram showed rather low T waves in the three limb leads, and a deep Q wave, with an upright T wave, in Lead 4. The hemoglobin was 38 per cent and the stools were guaiac positive. A few months later the patient suffered from a severe hemorrhage from a carcinoma of the colon, followed by collapse. A few hours after this he was seized with severe substernal pain. An electrocardiogram revealed the typical pattern of posterior infarction. After recovery from the cardiac infarction, the carcinoma was operated on and the patient recovered.

Several writers (Menard and Hurxthal,[15] Balfour,[16] Randall and Orr,[17] Friedberg and Horn,[18] Herrick,[19] DeSanto,[20] Saphir, Priest, Hamburger and Katz,[21] Master, Dack and Jaffe[22] and Boas[23]) have described coronary occlusion following operation or shock. Blumgart, Schlesinger and Zoll[24] described 11 cases in which multiple fresh coronary occlusions occurred following shock. One of these cases was that of a sixty-nine-year-old man who suffered from a bleeding gastric ulcer.

The material to be presented divides itself into two groups. Group 1 consists of 4 cases in which actual infarction of the myocardium was present. Group 2 includes 6 cases in which the patients were precipitated into cardiac failure by hemorrhage. The following case is illustrative of Group 1.

G. G. (B. C. H. 896,396), a 55-year-old man, was first seen at the Boston City Hospital in August, 1937, because of periodic bouts of epigastric distress associated with nausea and gaseous eructations and relieved by food or alkali. In addition, shortly before entry, the patient felt weak and had noticed a few tarry stools. X-ray examination confirmed the diagnosis of duodenal ulcer. At that time, the lowest hemoglobin determination was 75 per cent and the lowest red-cell count was 4,110,000. The patient was placed on a Sippy regime, with relief of the symptoms; the stools, which were positive for occult blood, became guaiac negative. He was sent home, to be followed in the Out-Patient Clinic. Except for an episode of bleeding in 1940, he did well on his diet until September, 1942, when he was again admitted to the hospital. He complained of severe epigastric pain of 1 day's duration, associated with the passing of three copious tarry stools and the vomiting of 500 cc. of dark-red blood. The patient stated that for the last several years he had had high blood pressure and dyspnea, and substernal pain on moderate exertion.

While the patient was being questioned and examined, he was suddenly seized with sharp substernal pain, together with severe pain in the right elbow. He became cyanotic and dyspneic and the skin was cold and clammy. The heart sounds were faint and rapid. The heart was slightly enlarged to the left. The blood pressure was 90/50 and the pulse 150. Many moist rales were heard over the lung bases. The peripheral veins were collapsed.

Numerous blood transfusions were given, and the red-cell count, which was 1,500,000 on admission, rose to 3,810,000. The patient improved somewhat and the blood pressure rose to 160/110. An electrocardiogram showed evidence of recent myocardial infarction. The patient then developed bronchopneumonia and, despite chemotherapy, died on the 7th day following the onset of the severe cardiac symptoms.

Autopsy. The heart weighed 510 gm. The myocardium of the anterior and lower portion of the interventricular septum and the lower and anterior portions and the apex of the left ventricle were mottled with several large, pale-yellow gray areas with hemorrhagic borders. Microscopic sections showed the muscle cells in these areas to be undergoing dissolution, with beginning phagocytosis of the muscle cells. There was moderate infiltration by polymorphonuclear cells. The coronary arteries showed marked atherosclerosis. There was a recent thrombus in the anterior descending branch of the left coronary artery, beginning a few millimeters from its origin and extending for a distance of 1 cm. There was a 1-cm. ulcer within a deep crater on the posterior wall of the stomach 0.5 cm. above the pylorus. The mucosa of the stomach was bloodstained, and changed blood was found throughout the intestinal tract.

There were 3 other cases in this group. They were similar in that myocardial infarction and marked atherosclerosis of the coronary vessels were demonstrated at autopsy. In 1 case, there was a thrombus superimposed on a ruptured intimal plaque. In 2 cases, no actual point of complete occlusion of the artery could be demonstrated. In 2 of the 3 cases, the bleeding was due to duodenal ulcers. In the third case, acute ulcers at the cardia of the stomach were the source of the bleeding.

The following case is typical of the cases of Group 2, in which cardiac failure followed hemorrhage.

A 66-year-old man gave a 10-year history of epigastric pain following meals, which was relieved by soda. On the day of entry he passed a large, tarry stool, with weakness and subsequent collapse and vomiting of 500 cc. of bloody fluid. On entry the heart was slightly enlarged to the left and

MEDICAL PROGRESS

DIABETES MELLITUS

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IN THE following remarks on the progress in the treatment of diabetic coma and of pregnancy in diabetes I have confined myself to data from the George F. Baker Clinic for four reasons: they are more favorable and based on larger numbers of cases than are those reported elsewhere; it would be unfair to cite comparative data from other sources, because such reports often represent the results of treatment by many doctors, possibly with different ideas, on different services in a hospital and where, perhaps, the senior members of the staff are able to take a less active part in the management of the individual case; in some hospitals, facilities for laboratory work are inadequate, particularly at night and on Saturday afternoons, Sundays and holidays or the expense of such tests is so considerable that the medical staff is handicapped in securing or feels averse to ordering the same; and, finally, the classification of what diabetic coma is varies according to the author reporting the data. Regarding the last, we believe that a carbon dioxide level of 20 vol. per cent (8.8 millimols per liter) or below is the greatest common divisor. We know the term "unconsciousness" is inaccurate, because so often diabetic patients are unconscious from other causes than ketosis and because the term depends so much on the attitude and tests applied by the examining physician. A recent study[1] of causes of death of 307 diabetic patients in the period 1932 to 1942 on whom autopsies were performed, supports this statement, "The example of a cerebral hemorrhage found at autopsy as a cause of death in a case clinically diagnosed as a diabetic coma is a not infrequent occurrence."

DIABETIC COMA

The secret of success in the treatment of diabetic coma is the early and adequate administration of insulin. This is exemplified by experience based on 603 cases treated at the George F. Baker Clinic of the New England Deaconess Hospital between May 23, 1923, and December 31, 1944. Between August 21, 1940, and December 31, 1944, there were more than 9000 admissions for diabetes, with 158 deaths, and among these admissions there were 141 patients in the coma group (blood carbon dioxide 20 vol. per cent or less), with 2 fatalities. Treatment from beginning to end has been essentially the same for all cases except that the first 50 coma patients treated in the earlier period received an average of 83 units of quick-acting insulin in the first three hours, and the last 141 an average of 206 units.†[2] Of the former group 18 per cent died, and of the latter, 1.4 per cent.

During all these twenty-one years, diagnostic laboratory aid has been efficient and prompt — day and night, Saturday afternoons, Sundays and holidays. At a hint of an approaching coma admission the nursing and medical staff, young and old, are alerted, and the rule holds that, after the patient arrives, if there appears a possibility at any time until complete recovery that death might ensue within two hours, two of the older group must be in actual attendance or in close consultation.

The size of the first dose of insulin is usually determined by the clinical estimation of the degree of acidosis, bearing in mind that in a patient with a relatively recent onset of the diabetes, particularly in a child, with acidosis of short duration and with unconsciousness absent, slight or not profound, less insulin suffices than if one is dealing with diabetes or acidosis of long duration and deep unconsciousness. It is in such cases that judgment counts and physicians with large experience dare to give larger doses of insulin than those with somewhat less intimate contact with coma cases. The first dose is usually between 50 and 100 units.

Within thirty to forty-five minutes after entrance, doubt about future treatment is removed because reports of the sugar and diacetic acid in the urine and of sugar and carbon dioxide in the blood are available and, shortly after that, reports of the urinary albumin and sediment and the nonprotein nitrogen of the blood. Subsequent dosage of insulin and its frequency vary with the height of the blood sugar and the depth of the carbon dioxide. Usually the entrance dose of insulin is immediately repeated and again repeated in another hour, that is, about two hours after admission, by which time later reports of the blood sugar and carbon dioxide furnish the therapeutic indications. A few cases recover with a total of less than 100 units, especially if the referring physician has given insulin before arrival, whereas an insulin-resistant patient whose customary daily dose of insulin is 400 units may require 2500 units. As previously mentioned, the average dose administered in the last 141 cases in the first three hours — the period that counts — was 206 units.

Intravenous physiologic saline solution is begun immediately on arrival, because all coma patients

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†The average of 216 units for 123 cases in the last group was reduced to 206 units by the addition of 18 cases recently treated. This series included 15 children or patients under 20 years of age several of whom had received large doses of insulin before arrival at the hospital.

are dehydrated. Seldom are less than 2 liters given in the first six hours, and only once has as much as 11 liters of fluid been administered subcutaneously, by vein, by rectum and by mouth in the course of twelve hours, as occurred in Case 15791, that of a patient who recovered under the joint care of Drs. Root and Riseman at the Beth Israel Hospital.[3] This patient, profoundly unconscious, became anuric after the administration of glucose solution. She remained anuric for *nine hours* but recovered when constant intravenous salt solution was given for eleven hours. This patient is not included in our series.

Lavage of the stomach is almost invariably carried out soon after entrance, but the delicacy with which this act must be performed on a patient almost in extremis should be realized. We have never regretted emptying the stomach of a patient in diabetic coma, but despite knowledge gained through practice over many years a reluctance and a delay on various occasions to adopt this procedure have brought embarrassment later when the patient, contrary to our preconceived notions, has vomited unexpectedly large quantities of bloody gastric contents. In the long run it is safer to empty the stomach with a tube, as a rule inserted intranasally, than to have the patient regurgitate and aspirate fluid and undigested food into his lungs.

The bowels are emptied by enema, but again, one should be mindful of the weakened state of the patient.

Warm blankets and accessory heat cautiously applied are utilized to bring the temperature of the body up to normal from its customary subnormal level. Fever spells a complication.

The determination of the blood carbon dioxide content is of great value in the estimation of the patient's condition. Some excellent writers depend in large measure for diagnosis and treatment on the presence, degree or absence of consciousness. Unconsciousness is a variable feature and rests on a clinical impression. Its existence varies to a considerable extent with the response of the patient to stimuli of sound or pain, and such stimuli vary from doctor to doctor. Moreover, the patient may be deaf, or the unconsciousness due to a cerebral hemorrhage, with an accompanying slight acidosis or even actual diabetic coma, and it is not rare in infections with children. The level of the carbon dioxide is a concrete fact and not open to clinical error. More and more patients are sent into the hospital for diabetic coma with conditions that have no relation to it; in such cases, knowledge concerning the carbon dioxide level is extremely helpful. Whether or not one believes in the value of the carbon dioxide determination as a therapeutic indication, it remains in our minds as the best diagnostic criterion, the greatest common divisor of all the symptoms and signs of diabetic coma and the best basis for the comparison of different methods of treatment.

Alkalies have not been given to our patients since 1917, and that type of treatment will not be discussed. Indeed, in few clinics are they generally advocated today, particularly in appreciable amounts.

Two of our 141 patients in coma died. The first (Case 22682) was a nineteen-year-old girl, admitted on April 10, 1943, diabetes having first been discovered in the same month. Acidotic symptoms began thirty hours previously, in the course of a sinus infection. When she was transferred to us from another hospital because of anuria, she was moribund, her pulse was 140, and the temperature 101.4°F., and she had received 100 units of insulin. With the administration of more insulin and 5000 cc. of saline solution the blood sugar fell from 534 mg. to 165 mg. per 100 cc. and the carbon dioxide rose from 12 to 21 vol. per cent. She was seen by various specialists, but operation was deemed inadvisable, and she died six and a half hours after admission. Autopsy showed purulent infection of both the sphenoid and ethmoid sinuses, early bronchopneumonia and atherosclerosis of aorta. Death was caused by sepsis due to a hemolytic *Staphylococcus aureus*. The other patient (Case 24095) entered with a coronary thrombosis of twelve hours' duration and lived an hour and a half; the autopsy showed occlusion of both coronary arteries.

A third patient (Case 23935) is not included in our series. He was 19 years old and had had diabetes for two years. He entered following coma but without the presence of acetone or diacetic acid in the urine and with a blood carbon dioxide of 23 vol. per cent. He was unconscious and had been given elsewhere 400 gm. of glucose in the first twelve hours of treatment. He was not suffering from severe acidosis, but from glucose administration. The blood sugar was 680 mg. per 100 cc. He received 320 units of insulin, with the result that the blood sugar value at the end of six hours had fallen to 222 mg. and that the carbon dioxide level at the end of three hours had risen to 40 vol. per cent. He lived nine hours. Autopsy showed slight atherosclerosis of the aorta and early pulmonary congestion.

Glucose has not been used in our clinic in the early stages of the treatment of diabetic coma since 1917. It is administered as soon as the amount of sugar in the blood approaches a nearly normal level and the urine is nearly or quite sugar free. Our design is to provide during the first twenty-four hours of treatment that the carbohydrate intake by mouth or vein shall be not less than 100 gm.

Glucose is advocated by some clinicians on the basis that it will be oxidized and that its oxidation will favor the oxidation of beta-oxybutyric acid and its derivatives. The experiments or remarks of Soskin and Mirsky are cited to support this contention. Our ideas can perhaps best be presented in the form of questions and answers.

Is the body of the patient in diabetic coma lacking in carbohydrate? It is not. Table 1 shows a comparison by Dr. H. F. Root[4] of the carbohydrate in a normal man, weighing 70 kg. with that of a patient of similar weight in diabetic coma with a blood sugar level of 700 mg. per 100 cc. Soskin[5] used the same figures for normal persons, but he did not include the skin. In coma he considered that the blood

TABLE 1. *Carbohydrate Stores in a Normal Person and Patient with Diabetic Coma.*

SOURCE	NORMAL		DIABETIC COMA	
	CONTENT	TOTAL	CONTENT	TOTAL
	%	gm.	%	gm.
Muscle, 30 kg. (glycogen)	0.6	180	0.3	90
Liver, 1800 gm. (glycogen)	6.0	108	1.0	18
Skin (glucose)	0.08	4	0.56	28
Extracellular fluid, 21 kg. (glucose)	0.08	17	0.70	146
Totals		309		282

sugar was 0.35 mg. per 100 cc. and that the reduction of the glycogen stores might be greater than that shown in the table.

According to the respiratory quotients of 0.68 and 0.69 observed and reported by Root and Carpenter,[6] no significant quantity of carbohydrate is oxidized during diabetic coma. The respiratory quotient was not raised by glucose alone, but was raised when sufficient insulin was given.

Is glucose injected into the vein burned any better than glucose already present in the body? No. Glucose given by vein is no better oxidized than the glucose already present in excess. Indeed, when Root and Carpenter[6] compared in normal students the effects of 50 gm. glucose by vein and by mouth, the increases in carbohydrate combustion during the two and a quarter hours after intravenous injection were a little less than those when the glucose was given by mouth, the respective averages for four subjects being 9.0 gm. and 10.6 gm.

How much carbohydrate does a man weighing 70 kg. burn an hour when at rest and when at moderate work without food? Such a man burns 5 to 6 gm. at rest and may burn as much as 30 gm. in an hour at moderate work. In hyperthyroidism, the former figure only rises to 6.4 gm.[7, 8]

How much carbohydrate must be burned hourly to avoid acidosis? This is variable. The diabetic patient who assimilates 100 gm. of carbohydrate per 24 hours shows no significant acidosis.

What has recently come from Soskin's pen on this subject? Soskin's[5] recent article emphasizes the primary place of insulin in the treatment of diabetic coma, but he states that in the first twenty-four hours such a patient needs 500 gm. of carbohydrate to return the glycogen stores to normal and to provide 50 per cent of the 2100 calories required in that period. Actually, it is known that the patient in diabetic coma should have his total metabolic rate reduced by rest in bed and by a diet consisting of not over 20 calories per kilogram, or approximately 1400 calories. As soon as serious acidosis is relieved, the carbohydrate stores can again be replenished.

What has Mirsky said about glucose in diabetic coma? He[9] writes as follows:

> It must be emphasized that a distinction should be made between hyperglycemia due to a high carbohydrate intake and that due to endogenous sources. In the former, the high blood sugar merely reflects the character of the diet and indicates that an increased amount of substrate is available for deposition in the liver; in the latter, the hyperglycemia represents a disturbance of regulation of such a degree that formation of dextrose and breakdown of glycogen are accelerated. Needless to say, excessive amounts of carbohydrate, such as we used, are contraindicated as a therapeutic procedure because of the polyuria and resultant loss of weight on the one hand and the possible danger of pancreatic exhaustion on the other.

Why is the administration of glucose harmful in diabetic coma? There are several reasons. In the first place, it obscures an estimation of the progress of the case toward recovery, because the blood sugar level is no longer a measure of adequate insulin dosage. Secondly, it may injure the liver.[10] Thirdly, it may provoke anuria, or if not burned, may deplete the body of fluid. Finally, in 17 cases of diabetic coma seen by Dr. H. F. Root[11] in consultation, submitted to him for review or published in extenso in the literature in which the patients received large amounts of glucose early in the course of the attack and before adequate insulin had been given, the mortality was 100 per cent. Of course, 25 or even 50 gm. of glucose will not kill the patient who first receives insulin in amounts sufficient to utilize the excessive glucose in the blood and extracellular fluid of the body, as indicated by a decline of the blood sugar to a normal level.

Dr. John P. Peters, of New Haven, in a personal communication says that his initial priming dose of glucose is approximately 25 gm. along with insulin and thereafter, including the first dose, is kept up at the rate of about 10 gm. per hour until the blood sugar begins to decrease, when the carbohydrate is increased and the insulin is diminished according to the condition of the patient.

To this discussion I am allowed to add a pertinent comment by Dr. Charles H. Best, of Toronto:

> Although there are a number of conditions characterized by a low level of glycogen in the liver in which there is deficient oxidation of carbohydrate in the body, there are, on the other hand, conditions that deplete liver glycogen, such as severe muscular exercise and the administration of thyroid hormone, which are certainly not associated with impairment of carbohydrate oxidation. In other words, it would not appear to be a low level of liver glycogen per se that interferes with the oxidation of carbohydrate.

ALLOXAN

Alloxan still holds the center of experimental investigation in diabetes mellitus. The prominence given to it in the progress report of a year ago[12] is justified by the articles about it that have appeared

in Scotland, Argentina, Chile, England, India, Mexico and Canada as well as in the United States. In the following section an attempt is made to present recent work that has extended knowledge concerning the effects of this diabetes-provoking chemical, which has such a highly selective action and affinity for the beta cells of the islands of Langerhans — all told, they comprise only about 0.007 per cent of the weight of the entire body, the equivalent in weight of a lump of sugar — that it destroys them within a few hours, leaving the remainder of the body intact.

In recapitulation it may be said that alloxan is the ureide of mesoxalic acid. When 200 mg. per kilogram of body weight are injected intravenously into a rabbit, hyperglycemia occurs for one or two hours, followed by extreme hypoglycemia, which, if untreated with glucose or food, usually results in the death of the animal within twenty-four hours. If the animal is prevented from dying in hypoglycemia, diabetes results. Autopsy reveals extensive necrosis of the islands of Langerhans, with destruction of the beta cells but sometimes without notable injury to the alpha cells. The acinar tissue and other parts of the body escape injury unless the dose of alloxan has been excessive. Such animals can be maintained with insulin for over a year, exhibiting severe diabetes with lipemia and acidosis. Similar results have also been obtained with rats and dogs.

Hughes, Ware and Young[13] have produced a state of hyperglycemia followed by hypoglycemia, similar to that which is observed after an injection of alloxan, by the injection of adrenalin and an amount of protamine zinc insulin equivalent to that estimated to be present in the pancreas of a normal rabbit, namely, 10 units per kilogram of body weight. This suggests that the initial hyperglycemia may be due to adrenalin excretion and that the hypoglycemia is not caused by an overactivity of the beta cells, as was once surmised, but rather by the liberation of preformed insulin. This explanation received additional support by the fact that Hard and Carr[14] and others[15] noted that the islands of Langerhans begin to show pathologic change within five minutes after the injection of alloxan. More conclusive evidence was presented by an ingenious experiment of Goldner and Gomori,[16–18] who removed the adrenal glands or destroyed the adrenal medullas of rabbits by intramedullary injections of formalin. A diabetogenic dose of alloxan was then given, and in no instance did initial hyperglycemia develop. Severe hypoglycemia occurred, presumably enhanced by the lack of adrenal counter-regulation factor. They conclude that adrenal stimulation of glycogenolysis is involved in the production of the initial transitory alloxan hyperglycemia. Beta-cell degeneration occurs within the first hour and precedes the hypoglycemia, which usually develops only after four or five hours. Whenever hypoglycemia develops, diabetes follows if the animal survives. On the other hand, Banerjee,[19] although losing three rhesus monkeys with hypoglycemia following injections of 300 mg. alloxan per kilogram, observed that three others developed diabetes, although their blood sugar levels remained persistently high.

Degeneration of the beta cells with the decrease in insulin production has been demonstrated by insulin assay of the pancreases of Goldner and Gomori's dogs with alloxan diabetes of eighteen, thirty and sixty days' duration. The pancreases of these dogs contained only about one fourth of the 2 to 3 units of insulin per gram contained in those of normal dogs.

Ridout, Ham and Wrenshall[20] have shown in both cats and dogs that the insulin content of the pancreas did not fall appreciably until most islet cells were found by histologic examination to be dead. In other experiments they found that alloxan did not exert a hypoglycemic effect in depancreatized dogs or in dogs previously made diabetic with alloxan. (See also Haist[21] for a comprehensive review including nearly two hundred citations covering the whole question of the insulin content of the pancreas and the factors affecting it.)

Abolition of the initial hyperglycemia subsequent to an injection of alloxan does not prevent the development of alloxan diabetes.[16–18] This is in sharp contrast to the diabetes produced by injections of anterior pituitary extract or by partial pancreatectomy, in both of which the diabetes is prevented if hyperglycemia is counteracted by insulin, phloridzin or starvation.

Bailey and Bailey[22] produced diabetes in rabbits with 200 mg. of alloxan per kilogram body weight in a single dose and also with repeated injections of 40 mg. per kilogram in a succession of seven to thirteen doses over a period of one to three weeks. In the latter animals histologic examination revealed a variety of changes in the islets of Langerhans. Some cells revealed hydropic degeneration, which in many instances is known to be reversible, whereas other cells showed irreversible changes and still others were normal. They report the occurrence of diabetic cataracts in both rabbits and rats and suggest that the administration subcutaneously of 200 mg. of alloxan per kilogram is a feasible method of producing diabetes in rats. Carrasco-Formiguera[23] not only observed a marked variation in the severity of alloxan diabetes in dogs but also reports a recovery from the diabetes. One dog, after exhibiting mild glycosuria and hyperglycemia for a few days as a result of an injection of alloxan, at which time it showed a mildly diabetic dextrose-tolerance test, gave a normal sugar-tolerance test forty-two days after the alloxan injection. This animal was therefore cured after a mild but unmistakable diabetes.

Kennedy and Lukens[24] point out the differences in the susceptibility of individual animals and of

different species to alloxan. Like Hard and Carr and Goldner and Gomori, they found that an animal refractory to alloxan usually does not respond to successive doses. They noted incidentally that animals — dogs, cats and rabbits — under barbiturate anesthesia, when injected with effective doses of alloxan, died; but others[25] have found it possible to produce alloxan diabetes in such rabbits by the injection of a diabetogenic dose of alloxan. Kennedy and Lukens noted no increase in mortality with light ether anesthesia. These authors also emphasize that alloxan is effective in rabbits when given intravenously but ineffective when administered subcutaneously or intraperitoneally, which suggests that it is rapidly altered when in contact with the tissues. In the rat, however, it is effective when given subcutaneously or intraperitoneally.

The rabbits of Kennedy and Lukens excreted 15 to 60 per cent of the available glucose of the diet, and the glycosuria was reduced by fasting. In 4 rabbits there was no evidence of improvement in the diabetes when the diabetes was controlled by insulin. Contrary to the experiments of Bailey and Bailey,[22] they noted no cataracts in rabbits made diabetic by alloxan after a duration of six weeks or longer.

They also observed that alloxan does not inactivate insulin in vitro. They state that hydropic degeneration was observed post mortem in the islet tissues of 2 rabbits with diabetes of one to two months' duration. This is ascribed by them to the effect of hyperglycemia on the beta cells that escaped destruction by alloxan.

In an article on the morphologic and physiologic changes of alloxan diabetes in the rabbit, Bailey, Bailey and Hagan[15] emphasize the specificity of action of alloxan, describe the pancreatic-islet changes at intervals after its injection, citing changes even after five minutes, and state that these changes are degenerative from the beginning. Only a certain percentage of alpha cells remain intact, as compared with the lesion in experimental pituitary diabetes, in which there is no destruction of the alpha cells. They observed that the lesions in the kidney of the alloxan diabetic rat were severer than those in the rabbit, all changes in rabbits outside the pancreatic islets being minimal. The lack of cellular response to the necrosis of the islands is remarkable. In almost all other forms of necrosis, neutrophils may be seen at one stage or another. This unusual response to alloxan, therefore, offers a biologic problem of considerable interest. The lesions that were produced by small doses of alloxan resembled all the well-known lesions of the islands in human diabetes. In addition the histologic lesions in the different phases of the blood sugar curve represent one continuous process.

Further discussion of the histologic changes in alloxan diabetes has appeared from the Pathological Department of the University and Western Infirmary, Glasgow.[26] These authors, too, noted that definite histologic changes can be recognized in the islands in about an hour and may be pronounced in three hours, when some beta cells appear to be necrosed. They also remark:

> With doses of 50 mg. per kilogram the beta cells sometimes show degranulation, but little necrosis, at twenty-four hours: the appearances are consistent with abnormal increase of function. After these smaller doses islet changes may be only slight and focal in distribution. Alpha cells are less prone to the necrobiotic changes than beta cells and, from early states, may be enlarged with apparent increase of granules when the beta cells are necrosed or exhausted: this observation suggests some difference in function of the two types of cell. A temporary hyperglycemia almost always occurs in the first two hours where there is any damage to the islets.

Hooded rats were supposed to be resistant to alloxan, but Duff and Starr[27] have found that alloxan injected subcutaneously into these animals in doses of 175 to 350 mg. per kilogram of body weight regularly produced rapid selective necrosis of the islands of Langerhans and characteristic fluctuations of the blood sugar level. Histologic alterations in the islets of Langerhans conformed to those described with white rats, but in addition, a great increase was observed in the activity of mitotic division in the acinar cells during the first twenty-four hours after the injection of alloxan. Hypoglycemic convulsions were not observed. The urine collected during the first six hours was pink, resembling the color that results when alloxan is allowed to evaporate in air. With large doses of alloxan, and sometimes with small ones, the blood sugar rose at times to 800 to 1450 mg. per 100 cc., with death in a state suggestive of diabetic coma, accompanied by massive glycosuria and acetonuria. With smaller doses the animals usually survived for weeks or months without treatment, with blood sugar levels of 300 to 500 mg. per 100 cc. They, too, observed that at one hour after injection histologic changes in the islands were apparent. Most of the destruction occurred in the beta cells, but there were also some necrotic alpha cells. In addition there was a notable increase in the mitotic activity of the acinar cells. With the exception of slight degenerative changes in the convoluted tubules of the kidney and slight fatty metamorphosis of the liver, there were no significant alterations in other organs. Sections of the livers from diabetic animals were lacking in glycogen. Glycogen in the heart muscle was not more than normal, but glycogen in the renal tubular epithelium, especially that of the loops of Henle, was demonstrated in several animals.

Lackey, Bunde, Gill and Harris[28] recall that the glycogen in the heart of a dog or a cat is increased by pancreatectomy. Since both exocrine and endocrine secretions are eliminated by pancreatectomy, they investigated the glycogen problem in rats previously made diabetic with alloxan. The alloxan-treated animals, as compared with the controls, showed a statistically significant increase in glycogen

content of the heart muscle and a statistically significant decrease in that of the liver and skeletal muscle. Rappaport[29] claims that brain slices of alloxanized rats, like those of normal rats, consume more oxygen when glucose is present in the medium than when it is not. The evidence indicates that in the rats suffering from this form of diabetes there is no impairment in the ability of the brain to oxidize sugar.

Koref, Vargos, Rodriguez and Telchi,[30] working in Chile, have produced necrosis of the islands of Langerhans, where others have failed, with the use of alloxantin, which can be regarded chemically as an oxidation product of uric acid or a reduction product of alloxan. This finding has been confirmed by Bailey and Bailey.[31] Alloxan dissolves fairly well in cold water, whereas alloxantin has a low solubility in cold but is fairly soluble in hot water. Another distinguishing mark between the two is that alloxan gives a white precipitate with barium hydrate, and alloxantin a violet one. They therefore used solutions of 1.0 and 2.5 per cent alloxantin at about 50°C. in doses of 70 to 230 mg. per kilogram of body weight. The smaller concentration was the more toxic. Many of the rabbits died before diabetes developed, but others had typical diabetes. Histologic examination showed, as with alloxan, lesions in the islands of Langerhans — cellular degeneration and necrosis, marked diminution of the beta cells and, in cases of long duration, a diminishing amount of islet tissue. They state:

> It would appear that alloxantin may produce experimental diabetes, but there are apparently certain differences from the effects of alloxan. First of all there is the paradoxical effect that the lower concentrations, even administered in small doses, are more toxic than the larger doses in higher concentration. This may be explained by the supposition that the alloxantin, like alloxan, is mainly a capillary poison. If such a compound is administered in higher dilution, its diffusibility will be increased, especially in cases of relatively insoluble substances. Consequently it could paralyze more rapidly the capillary system. Higher concentrations with tendency to crystallize may act more slowly, developing rather the symptoms of subacute intoxication. The second fact is that none of the animals treated in our experiments with alloxantin developed hypoglycemic shock, although we could demonstrate that the blood sugar figures reached a very low level.

Thorogood[32] injected 50 rats subcutaneously with 200 mg. of alloxan per kilogram of body weight and found that 10 developed diabetes, 10 were not affected and 30 died. Others[21] observed that 12 of 15 rats developed diabetes with this dosage subcutaneously.

Banerjee[19] reports the production of alloxan diabetes in 3 of 6 monkeys given 300 mg. of alloxan per kilogram of body weight. The remaining 3 died in hypoglycemia.

Recently, Leech and Bailey[33] reported a test for the detection of alloxan in the blood. Using this test they demonstrated that alloxan reaches its highest level at the end of the injection, following which it rapidly decreases, with a complete disappearance in five minutes. This coincides with the finding of Goldner,[16–18] who reports that, if a part of the pancreas is temporarily deprived of its blood supply for five minutes after the injection of alloxan and the temporary blood ligatures are then released, that part of the pancreas escapes injury, showing that the damage occurs within the first five minutes. Leech and Bailey further found the reduced glutathione in the blood was markedly decreased, in some cases to zero, immediately after the injection of alloxan, which suggests an interaction of these two substances. Another sulfhydrol compound, — thionine, — in the 2 cases tried, seemed to follow a similar change.

Since the injection of both anterior pituitary extract and alloxan may produce diabetes in animals, it seemed important to find whether alloxan acted through the pituitary gland. Bailey[34] proved that alloxan did not exert its diabetogenic effect in this way, since hypophysectomized rats given alloxan developed diabetes, with characteristic necrosis of the islets of Langerhans.

Pregnancy

Recent publications indicate that the obstetrician and the internist now agree that, whereas the maternal mortality in pregnant diabetic women has been low, the fetal mortality has been high, from 30 to 60 per cent, depending on the duration of the pregnancy.[35–37] Between January, 1936, and January, 1945, a study of 210 consecutive pregnancies in diabetic women was made at the George F. Baker Clinic.[38] In this series 209 mothers and 176 babies survived. An analysis of these cases indicates that a high fetal mortality is preventable.

Maternal, obstetric, chemical and fetal abnormalities characterize pregnancy in the diabetic patient. Thus, diffuse vascular disease and hypoovarianism are frequent complications, and more often than not the pregnancies occur in physically and gynecologically aged patients. In the uncorrected course of diabetic obstetrics, early spontaneous interruption of the pregnancy occurs in 25 per cent of the cases, toxemia in 33 per cent, and breech presentations in 33 per cent. Uterine inertia is of common occurrence, and lactation rare. Chemical abnormalities include a low renal threshold for glucose, which favors the development of acidosis and hypoglycemia, water retention in the maternal tissues, amniotic sac and fetus and an imbalance of the sex hormones of pregnancy comprising a rise of chorionic gonadotropin and a fall of estrin and of progesterone, the last having been found in 70 per cent of our cases. Of the fetal abnormalities, overweight occurs in 80 per cent of the uncorrected cases, obesity, edema and splanchnomegaly being contributory factors. Excessive hematopoiesis of the liver and spleen and islet hyperplasia have been observed in nearly all fatal cases. Atelectasis is the

most frequent and important neonatal complication.

Although all these abnormal factors contribute to fetal mortality, the imbalance of the sex hormones of pregnancy appears to be the most harmful factor. In 58 cases in which the sex-hormone balance was normal there were no premature deliveries, 2 per cent of the patients developed toxemia, and 97 per cent of the infants survived. Among the 41 cases with an imbalance of sex hormones, 40 per cent of the patients delivered prematurely, about 50 per cent developed pre-eclamptic toxemia, and only 54 per cent of the infants survived. Estrin and progesterone were administered in 110 cases with the hormonal imbalance. Fifteen per cent of patients delivered prematurely. The incidence of toxemia in patients treated throughout pregnancy dropped to 5 per cent, and fetal survival rose to 89 per cent.

The therapy recommended is as follows: 1 or 2 gr. of Armour's thyroid daily, from the beginning of pregnancy; proluton in ascending doses, from the diagnosis of pregnancy to the sixteenth week, 5 mg. three times a week, from the sixteenth to the twentieth week, 5 mg. daily, from the twentieth to the twenty-fifth week, 10 mg. daily, from the twenty-fifth to the twenty-eighth week, 15 mg. daily, from the twenty-eighth to the thirty-second week, 20 mg. daily, and from the thirty-second to the thirty-seventh week 30 to 40 mg. daily; and stilbestrol likewise in ascending doses, from the twentieth to the twenty-fourth week, 10 mg. daily, from the twenty-fifth to the twenty-eighth week, 15 mg. daily, from the twenty-ninth to the thirty-second week, 20 mg. daily, and from the thirty-second to the thirty-seventh week, 30 to 40 mg. daily. The diet should include liberal quantities of carbohydrate and protein; salt should be omitted after the sixth month. Insulin is usually necessary before lunch and supper, in addition to the breakfast dose.

The time for delivery is the thirty-seventh week, and we believe that the method of choice is cesarean section, without medication and under spinal anesthesia.

The welfare of the infant is aided by oxygen incubation, mechanical stimulation, dehydration and drainage.

It does not seem illogical to believe that the vascular disease and hormonal imbalance of the young diabetic woman predispose her to the vascular disease and hormonal imbalance of pregnancy — a prematurely aging patient — and a prematurely aging placenta.

Statistics

A preliminary and round figure for diabetic deaths in the United States for 1943 is 37,000, a rate of 27.6 per 100,000.[39] New York leads with 43.6, Rhode Island follows with 43.0, and Massachusetts is third with a rate of 39.4. The percentage increase in the total United States for the three years 1930–1932, as compared with the three years 1940–1942, was 27 per cent. By states, Oklahoma and Arizona led with increases of 48 and 47 per cent, respectively; the higher rates, however, were only 15.2 and 11.9 per 100,000. The increases in New York, Rhode Island and Massachusetts were respectively 40, 27 and 38 per cent.

Rates for the industrial insured cases of the Metropolitan Life Insurance Company for the period 1939–1944 have varied from 27.4 per 100,000 in 1941 to 29.8 in 1940; the rate for 1944 was 27.6.

Diabetes Abstracts

Mention should be made of the great contribution to the diffusion of knowledge concerning diabetes that has been afforded by the joint publication of *Diabetes Abstracts* by the American Diabetes Association and the Eli Lilly Company. Four numbers appear yearly. They contain an exceptionally careful summary of all current papers on various aspects of the disease. The time thus saved to the physician is almost incalculable.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31081

PRESENTATION OF CASE

A fifty-four-year-old dishwasher was admitted to the hospital complaining of dyspnea, chest pain and rusty sputum.

The patient was well until about one month prior to admission, when he developed a persistent slightly productive cough following an upper respiratory infection. Five days before entry he developed generalized aches and pains, with malaise and a shaking chill. On the following day he experienced a second chill. He noted slight sharp pain in the right chest on inspiration and increasing dyspnea. Three days before entry he began to cough up rusty sputum.

The patient had had urgency and nocturia (two to three times) for several years, associated with difficulty in starting and a diminution in the force of the stream. He had had some dyspnea on climbing one flight of stairs, but there was no history of orthopnea, ankle edema or pain in the legs. He drank six to eight glasses of beer daily and whisky occasionally.

Physical examination revealed a well-developed and well-nourished, slightly cyanotic and dyspneic man appearing acutely ill. The skin was hot and moist. The pupils were somewhat irregular, and the fundi revealed slight tortuosity of the vessels, with arteriovenous nicking. Over the right lower lung field, more marked posteriorly, there were dullness, increased tactile and vocal fremitus, and diminished breath sounds. A Grocco's triangle was present on the left. The heart sounds were poorly heard. A marked aortic systolic murmur, accompanied by a thrill, was heard over the precordium, with maximum intensity about 5 cm. to the right of the sternum in the second intercostal space; it was transmitted to the right axilla and through to the back on the right. The abdomen was distended and tympanitic. The knee jerks were diminished, and the ankle jerks absent.

The temperature was 103°F., the pulse 110, and the respirations 24. The blood pressure was 100 systolic, 50 diastolic, in the right arm, 115 systolic, 70 diastolic, in the left arm, and 150 systolic, 70 diastolic, in both legs.

Examination of the blood revealed a red-cell count of 3,370,000, with 12.3 gm. of hemoglobin, and a white-cell count of 10,000, with 94 per cent neutrophils, of which 74 per cent were band forms. There were marked toxic granulations in the neutrophils. The urine had a specific gravity of 1.015 to 1.020, with a ++ test for albumin on admission but none thereafter; there was an occasional white cell and coarsely granular cast in the sediment. The stools were negative. The serum nonprotein nitrogen was normal, and the protein was 5.4 gm. per 100 cc., with an albumin-globulin ratio of 1.9. The prothrombin time was 24 seconds (normal, 18 to 20 seconds), and a cephalin flocculation test was negative. A bromsulfalein test showed 15 per cent dye retention. A sputum culture on admission revealed an abundant growth of Type 5 pneumococci, and a culture five days later showed a few beta-hemolytic and many alpha-hemolytic streptococci. Five blood cultures were negative. An electrocardiogram showed slight left-axis deviation, biphasic T_1 and T_2, flat T_3 and sagging ST segments in Leads 1, 2, CF_4 and CF_5, findings consistent with left ventricular strain and hypertrophy.

A roentgenogram of the chest revealed density in the right lower lung field. There appeared to be some widening of the right side of the mediastinum. The left lung field was clear. A repeat film three days later showed considerable density remaining in the right lower lung field; this was definitely within the lung. There was no other change.

Soon after admission the temperature spiked to 106°F., after which it ranged between 101 and 103, with occasional spikes to 104. Respirations averaged about 30. A tap of the right chest yielded slightly viscid, cloudy fluid containing fibrin; there were 50 cells per high-power field, 98 per cent of them being polymorphonuclears. Sulfadiazine therapy was instituted, following which the white-cell count fell to 3800. On the fifth hospital day, sulfadiazine was stopped and penicillin substituted. The white-

*On leave of absence.

cell count gradually rose to 12,000. A second thoracentesis, on the seventh hospital day, was productive of 650 cc. of viscid cloudy fluid having a specific gravity of 1.020 and a white-cell count of 4300, with 65 per cent polymorphonuclears. A culture of the fluid revealed *Staphylococcus aureus*. On the following day the patient complained of sharp pain on inspiration over the right lower chest, but no friction rub could be heard in this area. Fluoroscopy on the ninth hospital day revealed a wide mediastinum, an active expansile pulsation in the upper chest to the right of the midline, and what appeared to be collapse of the right lung at the base, with only a minimal amount of fluid. Examination of the chest showed decreased resonance at the right base, with diminished breath sounds and a few rales, especially posteriorly. There was dullness over the hilar region in the right posterior chest. Examination of the heart revealed the point of maximum intensity to be 10.5 cm. to the left of the midsternal line and 1.5 cm. beyond the left midclavicular line in the fifth intercostal space. The loud aortic murmur, as well as the thrill, was transmitted over the whole chest and into the neck, abdomen and back. It was loudest about a centimeter nearer the sternum in the upright than in the supine position.

On the fourteenth hospital day a therapeutic test with three 200-r doses of x-ray was begun. The patient showed no subjective change, and the temperature continued to range from 101 to 102°F. Penicillin was stopped on the twelfth hospital day, and 0.1 gm. of digitalis was administered three times daily. A roentgenogram of the chest on the eighteenth hospital day showed the density over the right lower lung field to have largely disappeared. Only a small amount of fluid remained in the right pleural cavity. The heart and mediastinum were markedly displaced to the right, and in the lateral view there was a suggestion of collapse of the greater part of the right lower lobe. The heart was enlarged, particularly in the region of the right ventricle. The aorta was tortuous and calcified, but there was no demonstrable evidence of aneurysm (Fig. 1). On the twenty-fourth hospital day, the temperature rose to 103.4°F. and the patient complained of intense pain over the right lower chest on inspiration. The breath sounds over the right middle lobe were absent, and the heart sounds were muffled. Fluoroscopy and roentgenograms of the chest revealed that the pulsations of the heart and aorta were much smaller

FIGURE 1.

than at the time of the previous examination. A large area of calcification was visible in the valvular area of the aorta, but there did not seem to be any appreciable aortic widening.

On the twenty-sixth hospital day the patient suddenly complained of intense and persistent chest pain; he died two hours later.

Differential Diagnosis

Dr. Wyman Richardson: "A fifty-four-year-old dishwasher was admitted to the hospital complaining of dyspnea, chest pain and rusty sputum." It sounds like lobar pneumonia, and the story of the illness immediately preceding entry also sounds like pneumonia.

The urgency, nocturia and so forth suggest that he had prostatic difficulty, but nothing more is said about it. In the story later on we find that he had a normal serum nonprotein nitrogen.

"He drank six to eight glasses of beer daily and whisky occasionally." I shall take that statement at face value, and I must say that it is not a terrific alcoholic history.

It is stated that there were diminished breath sounds with increased tactile and vocal fremitus. I doubt it; at least it does not sound reasonable.

"Grocco's triangle was present on the left." In other words, there was contralateral dullness.

The diminished knee jerks probably were of no consequence. The problem of obtaining ankle jerks in an extremely sick man makes that observation doubtful.

We still have evidence consistent with consolidation of the lungs, which is also consistent with pneumonia, and nothing so far to suggest that this patient did not have pneumonia. There is, however, the possibility of a heart lesion. The findings in the heart suggest calcareous aortic stenosis. The question is whether or not to take seriously the difference in blood-pressure readings in the two arms. To my mind the difference is not great enough, at least on the single observation, to put much stress on the finding.

The white-cell picture, with 94 per cent neutrophils, is certainly consistent with a fairly severe, acute pyogenic infection. Although we are not told what the other 6 per cent were, I assume that they were lymphocytes and that there were no eosinophils and no monocytes. The marked toxic granulations of the neutrophils can be overemphasized, but taken with the differential picture it is strong evidence in favor of an acute pyogenic infection. It is equally strong evidence against infection such as subacute bacterial endocarditis or septicemia without an acute exudative process, such as an abscess or something of that sort.

Dr. Benjamin Castleman: The remaining 6 per cent in the differential count was composed of 2 per cent large lymphocytes, 2 per cent small lymphocytes and 2 per cent monocytes.

Dr. Richardson: Although there are too many monocytes, the white-cell picture is consistent with and quite suggestive of pneumonia.

I might as well get the anemia out of the way. The red-cell count of 3,300,000 indicates a fairly definite anemia. I should like to point out that red-cell counts are not so accurate as they are thought to be. It is known that, when they are done by well-trained technicians on the same patient and repeated, they can vary as much as half a million or more in either direction. Of course, that does not mean that the error is always going to be that much. One cannot take a single observation too seriously; however, one must assume that this anemia meant something. That brings us down to the hemoglobin. In the general wards of this hospital it is presumably done by the Sahli method, and one should not be too impressed by the figure 12.3 gm. The Sahli method is full of snares and delusions — I fear that I am going to be hypercritical, even iconoclastic, about this. The Sahli test may vary as much as 25 per cent if one uses a yellow light, a filter light or daylight. Furthermore, the standards may fade, and although it is desirable frequently to calibrate them, they almost never are calibrated. With a faded standard the reading is obviously too high. This particular blood works out as a macrocytic anemia with a color index of 1.3.

Dr. Castleman: Five days after the first blood examination the red-cell count was 3,800,000; the differential white-cell count was 77 per cent neutrophils, of which 40 per cent were band forms with toxic granules, 12 per cent large lymphocytes, 8 per cent small lymphocytes and 3 per cent monocytes. A red-cell count done two weeks later was 3,600,000, with a hemoglobin of 10.5 gm.

Dr. Richardson: That would be a normochromic anemia.

The anemia should be explained, and I find it one of the most difficult things in this record to do. Anemia of course can occur with sepsis, but it usually follows chronic sepsis. One would expect it to be a little slower in developing. It is possible, however, that it was due to chronic sepsis. Anemia due to malignant tumors, provided the tumor is not in the gastrointestinal tract and associated with blood loss, or possibly a nutritional element, shows a considerable degree of regeneration. If one saw a smear with an anemia of that degree and then found numerous nucleated red cells or polychromatophilia with stippling or other evidence of regeneration, it would be suggestive of a malignant tumor. I do not believe that malignant tumor of itself produces anemia of this type. I do not know what the red cells looked like, as a matter of fact, and therefore one has to consider that this anemia may have been due to lack of liver principle or to some nutritional disturbance. The anemia of uremia may produce toxic granules, but we are told later on that the

patient had no uremia. One more point about the hemoglobin: I find that the most satisfactory method of hemoglobin determination, except for photoelectric measurement, is that given by the Tallqvist scale, using one of the old books. I expect that I shall hear a lot more about this statement later on.

DR. J. H. MEANS: I may say at this point that I think you are quite right. One has to add, however, that the person taking it should back up against the window and read it in daylight.

DR. RICHARDSON: It has to be read right away. The paper must be folded over double and the person should have his back to daylight. Using the old scales I can get a fair correlation with the photoelectric determination. It is not a falsely accurate test the way some of the others are.

"An electrocardiogram showed . . . findings consistent with left ventricular strain and hypertrophy." I shall accept that statement and make no further comment.

"Sulfadiazine therapy was instituted, following which the white-cell count fell to 3800." I still think that this story is consistent with an acute infection of the lung that had not resolved.

The fluid in the right lung was not a transudate; it appeared to be associated with infection in the lung and approached a definitely infected fluid of the empyema type, although it had not reached that stage. It certainly was not pus, but it seems as if it might well have been infected fluid.

There appears to be some question of aneurysm in this case, and I know that there is no report in the record of a Hinton test. I do not believe it was aneurysm. I assume that the test was not done or was negative.

DR. JOSEPH C. AUB: It was done and was negative.

DR. RICHARDSON: I suppose they gave him x-ray treatment as a last resort. It must have been a forlorn hope.

As I went over this story the first time, I did not quite gather the time relation. The patient apparently was well until a month prior to admission, and on the twenty-sixth hospital day he died. That means that he was sick for two months. To me this story is one of infection. I have to mention the possibility of aneurysm, but I do not believe that it was present. I believe that this man started off with pneumonia, which did not clear up, that he later had an infected pleura, with perhaps a localized empyema, that still later he had enough obstruction of the bronchus to cause collapse of the right lower lobe and that he ended up with an acute purulent pericarditis. In his heart, I believe that he had a calcareous aortic stenosis and also probably a good deal of calcium in the aortic arch. I do not believe that he had an aneurysm. In view of the length of the history, the anemia that I mentioned is consistent with chronic sepsis. The change in the blood picture in the last five days is difficult to explain, but it might have been an acute process turning into a chronic condition, perhaps as a result of drug therapy. I have nothing more to say.

I should like to have Dr. Robbins comment on the x-ray films. I might ask him first if he knows the answer; then I shall know how to interpret what he says.

DR. LAURENCE L. ROBBINS: I know the answer.

This is the film that was taken on admission, and all I can say is that the density of the right lower lung field could be due to fluid or to consolidation within the lung. The heart appears to be displaced to the right, and this shadow suggests widening of the superior mediastinum. At a later examination some of the density is definitely due to consolidation; I think, however, that there is still some evidence of fluid in the pleural cavity. The fact that we can see the bronchi suggests that there was a loss of aeration of the alveoli adjacent to the bronchi. Then as we go along a little farther, — if I remember correctly the department was being pushed for an opinion whether this could have been an aneurysm of the ascending aorta, — the process within the lung and the pleural cavity has cleared considerably. The heart and mediastinum remain considerably over to the right side. So far as we could determine at that time there was no widening of the aorta itself but the pulsations were considerably larger than one expects normally; we did not recognize the fact that there was some calcification in the valvular area. It is possible to see a large area of calcification in the region of the aortic valve. The heart has increased somewhat in size between these two examinations, representing a six-day interval. Even knowing the answer, I still cannot explain why the heart, mediastinum and aorta are displaced far to the right side. I do not believe that there is enough disease in the lung to explain this displacement.

DR. AUB: In the fluoroscopic examination the mass displaced to the right, which Dr. Robbins has stressed, pulsated twice in each beat, auricular and ventricular.

DR. RICHARDSON: I do not see much evidence of a localized empyema, but there may still be a localized area of infected fluid. My diagnoses are lobar pneumonia, which was resolving, calcareous aortic stenosis, acute pericarditis and possibly localized empyema.

DR. REED HARWOOD: The fact that this patient was sick for several weeks suggests that possibly he had something in the bronchial tree. Could he not have had a carcinoma of the bronchus to produce this bulge in the mediastinum?

DR. CHESTER M. JONES: Why did he have x-ray treatments?

DR. RICHARDSON: I was wondering about that.

DR. AUB: The patient had a thrill and a murmur as marked as any I have ever felt or heard. They extended almost to the right axilla and were much more marked when the patient was sitting up than

when he was lying down. That was the most striking thing about the examination.

He was first given sulfadiazine, which did not do any good, and then penicillin, which also was of no help; finally we had nothing else to offer except x-ray therapy, because of the remote possibility of Hodgkin's disease.

Clinical Diagnoses

Dissecting aneurysm, with rupture into pericardium.
Resolving pneumonia (Type 5).
Aortic stenosis.

Hemopericardium, with cardiac tamponade.
Massive pulmonary embolism, acute.
Thrombosis: right popliteal and femoral veins.
Resolving lobar pneumonia: right middle lobe.
Pulmonary infarct: left lower lobe.
Cardiac hypertrophy, left ventricular.

Pathological Discussion

Dr. Castleman: At autopsy this man presented an unusual picture. The heart was tremendous in size, weighing 800 gm., and showed marked left ventricular hypertrophy due to a marked calcareous aortic stenosis. Superimposed on the calcareous

Figure 2. *Mycotic Aneurysm of Aortic Valve Located between Aorta and Pulmonary Artery, Bulging into Right Ventricle and Rupturing into Pericardium.*

Dr. Richardson's Diagnoses

Lobar pneumonia (resolving).
Calcareous aortic stenosis.
Acute pericarditis.
Localized empyema?

Anatomical Diagnoses

Calcareous aortic stenosis.
Subacute bacterial endocarditis, aortic valve, with formation of a mycotic aneurysm and rupture into pericardium.

stenosis was a subacute bacterial endocarditis that had eroded the aortic wall in two places, one just behind a cusp in a sinus of Valsalva and the other just above the valve and near a large calcareous mass. I wondered if the constant rubbing of the calcareous mass on the aortic intima in this location might have been an added factor in producing the rupture. The perforation opened into the space between the aorta and the pulmonary artery, producing a large mycotic aneurysm, 6 to 8 cm. in diameter, with a tremendous bulge into the right

ventricle just beneath the pulmonary valve (Fig. 2). The aneurysm had invaded the ventricular wall but had not reached the endocardium, and had the patient lived longer, it might have ruptured into the right ventricular cavity, forming an artificial interventricular septal defect. This large mycotic aneurysm had ruptured superiorly into the pericardium, which at the time of autopsy contained a liter of blood. That was not the immediate cause of death, although, if we had found nothing else, we might have interpreted it as such. The enlarged heart shadow seen on the roentgenogram several days before he died undoubtedly was produced by the hemopericardium. The immediate cause of death was a massive embolus that filled the entire pulmonary artery and had extended into several branches within the lungs. These emboli came from thrombi in the right popliteal and femoral veins.

The lungs showed resolving pneumonia of the right middle lobe and a recent infarct in the left lower lobe, which probably occurred after the last x-ray film was taken. Nonhemolytic streptococci were grown from the contents of the aneurysm, from the vegetation and from the blood at autopsy.

DR. RICHARDSON: I made the flatfooted statement that the blood was not consistent with subacute bacterial endocarditis. I should like to modify that remark. I think that the first blood picture was not that of chronic sepsis but of acute sepsis, consistent with the pneumonia; the later blood report could be consistent with subacute bacterial endocarditis.

DR. CASTLEMAN: I cannot be sure when the mycotic aneurysm began, but I believe that it was there the day the patient came into the hospital. It was probably not so large, but it almost certainly had begun. The initial infection that led to the bacterial endocarditis may well have been the upper respiratory one over a month before admission. The hemopericardium occurred slowly during the last days of his life.

CASE 31082

PRESENTATION OF CASE

A seventy-four-year-old woman was admitted to the hospital with abdominal cramps and vomiting.

The patient had been in fairly good health until two days prior to admission when, after a light meal, she was suddenly seized with generalized abdominal cramps. This was followed by an episode of vomiting, which relieved the pain. During the night a second attack occurred. The abdominal cramps continued, and she was unable to take anything by mouth without vomiting. During this period, several enemas were productive of hard fecal masses; there was a small spontaneous bowel movement about an hour before admission.

The patient had had a hernia in the left groin since the age of ten. It had never been painful. About thirty years before entry she had attempted to wear a truss, but it was unsatisfactory and soon abandoned. About twenty-five years before admission the patient had had an acute episode of nausea, vomiting and upper abdominal pain diagnosed as gall-bladder disease. She recovered after about two weeks. Since that time she had had mild intolerance to fried and fatty foods and had avoided them. She had never had jaundice or tarry or acholic stools.

The patient required three pillows for sleeping but had never had dyspnea or edema. She had been told that she had high blood pressure and had had an episode of severe epistaxis one year before entry. She had been blind in the right eye for a year and in the left eye for six months, as a result of cataracts.

Physical examination revealed an obese dehydrated woman, vomiting frequently. Bilateral cataracts were present. The lips were cyanotic. The lungs were clear. The heart sounds were faint and irregular, and there was a soft systolic murmur over the pulmonic area. The abdomen was moderately distended, tympanitic and diffusely tender; no peristalsis was heard. A mass the size of a goose egg was present in the left groin and was believed to be a femoral hernia; it was tender and not reducible. Varicosities were present on both legs.

The temperature was 99°F., the pulse 86, and the respirations 24. The blood pressure was 200 to 216 systolic, 90 diastolic.

Examination of the blood revealed a red-cell count of 5,300,000, with 90 per cent hemoglobin, and a white-cell count of 14,400. The urine had a specific gravity of 1.014, with a ++ test for albumin, a + test for acetone and no sugar; the sediment contained innumerable white cells. The serum nonprotein nitrogen was 65 mg. per 100 cc., the protein 7.2 gm., and the chloride 93 milliequiv. per liter. The prothrombin time was 23 seconds (normal, 18 to 20 seconds).

A roentgenogram of the abdomen revealed numerous loops of dilated small intestine. There was a shadow of increased density overlying the sacrum (Fig. 1).

After several unsuccessful attempts, a Miller–Abbott tube was passed into the jejunum. The patient was given 6 cc. of Cedilanid intravenously. On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: Since Dr. McKittrick* has pointed out in a paper on acute intestinal obstruction that the one most important factor is the flat film of the abdomen, I think that we might start by looking at it.

*McKittrick, L. S. Diagnosis and management of acute obstruction of small intestine. *New Eng. J. Med.* 225:647-652, 1941.

DR. MILFORD D. SCHULZ: This film was made when the patient first came in, and you can see the widely dilated loops of small bowel. Over the sacrum is a shadow which, if it were in the right upper quadrant, I should call a gallstone. Since it is down over the sacrum I suppose it could be a calcified fibroid. If it were a gallstone I should expect some gas to be present in the liver or in the gall bladder.

in the opening sentence of the paper, "If one excludes strangulated external hernia, the diagnosis of which is easy and the treatment obvious. . . ." Sometimes the diagnosis is not so easy, and the treatment not so obvious.

But one must make a diagnosis. There are numerous factors that one would like to know about, as always in these exercises; some of them are probably

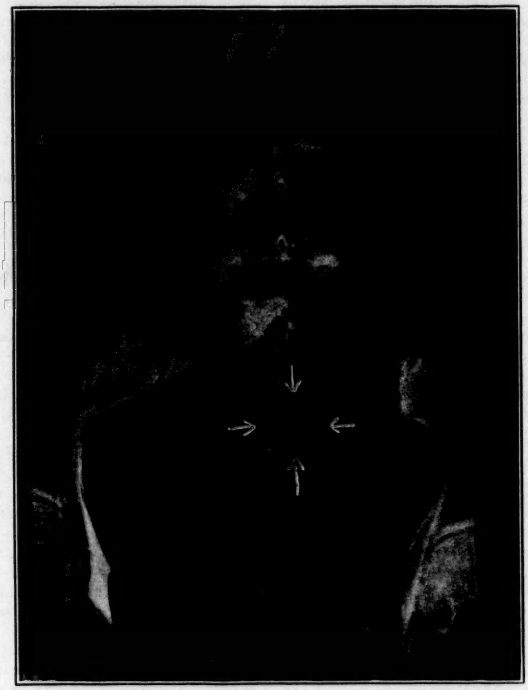

FIGURE 1.

DR. HAMLIN: There are obviously red herrings around, and that shadow is at least a fish.

DR. SCHULZ: It is interesting to know, too, that the gas stops at the dense shadow.

DR. HAMLIN: The diagnosis of small-bowel obstruction is obvious from the recorded physical examination and from the abdominal film. The story seems to lead rather clearly to a consideration of some sort of an incarcerated hernia as the cause of obstruction. Dr. McKittrick, as I mentioned before, in writing on intestinal obstruction, states not incorporated in the record, but some of them may be. One certainly would like to know more about the history and the character of the pain. Was the pain constant, although crampy in nature? Had it become more persistent, with crampy exacerbations, indicating that perhaps some form of strangulation of the intestine was taking place? It is of tremendous importance to differentiate simple obstruction and strangulated obstruction.

DR. BENJAMIN CASTLEMAN: Dr. Crystal, can you answer any of Dr. Hamlin's questions?

DR. DEAN K. CRYSTAL: We gained the impression that it was crampy pain, the severity of which had not changed during the illness.

DR. HAMLIN: The description by the patient leads one to believe that she was not a good informant.

DR. CRYSTAL: It was rather difficult to get the story.

DR. HAMLIN: One would like to know about the physical examination. Diffuse tenderness was described. In a person as sick as this it is frequently difficult to determine more than the fact that the patient merely reacts to abdominal pressure, but no more in one area than in another.

One would like to know about the presence of microscopic blood in the stool; a guaiac-positive reaction would perhaps aid in making the diagnosis. Was an abdominal tap done? The presence of blood in the fluid removed by the passage of a small-lumen needle into the abdominal cavity is quite significant; a negative examination is of no value.

DR. CRYSTAL: The stools were guaiac negative. An abdominal tap was not done.

DR. HAMLIN: From the description of the physical examination one would be justified in drawing the conclusion that there was widespread peritoneal irritation. Diffuse tenderness is certainly suggestive, because in simple obstruction, unless the vomiting itself produces enough muscle tenderness, localization is usually rather narrow. It is perhaps unwise, however, to draw any conclusion as to that. Certainly the laboratory examinations do not add to the picture; in an elderly dehydrated patient the white-cell count is frequently increased, even more than this.

I am not at all clear whether or not this woman had peritonitis. I am inclined to say that she at least had peritoneal irritation.

We now come down to the origin of the intestinal obstruction, the aforementioned red herrings being present. The first and most obvious one is the tender, irreducible lump in the left groin. Were this the site of an incarcerated hernia causing obstruction with the period of time that had elapsed, — forty-eight hours, — one would expect strangulation to have occurred. One would also expect the patient to complain of pain in that particular area rather than of generalized abdominal cramps. Also since it is so obvious, I am inclined, on the basis of what generally turns up at these meetings, to discard it, at least temporarily.

Then we have the lovely red herring in the x-ray film — a 4-cm. spheroid mass containing calcium, at which point it appears that the dilated bowel stops. That is interesting indeed. We have a history of an attack twenty-five years previously, which is consistent with gall-bladder disease. The patient had an aversion to fatty and fried foods, which is also consistent with gall-bladder disease, and it is perfectly possible that she had, over a long period of time, gradually eroded away an adhesion between the gall bladder and the small bowel and passed a stone into the small intestine, where it lodged and produced the obstruction. It is present on every film, but as Dr. Schulz has pointed out, it might also have been due to a calcified fibroid.

What are the other possibilities of small-bowel obstruction? At this patient's age, with the obvious heart condition that she had, — hypertension for a long period of time, — one must consider vascular occlusion in the mesentery of the small bowel, either embolism or thrombosis. If one tried to fit that into the story as given, I believe that it would be easier to ascribe the accident to thrombosis than to embolism. Although the onset was sudden, one gets the impression that she gradually became worse and that the degree of illness on entry was more attributable to the electrolyte imbalance and loss of fluids in general than to anything else.

There are a number of other things that can produce this picture, — volvulus, tumor and adhesions, — but I do not believe that we have to consider them as closely as the first three that I have mentioned, namely, hernia, gallstone ileus and vascular accident. There are many things against a vascular accident: the patient did not complain of pain in the back, she had a negative guaiac test on the stool, and there was no other evidence of blood. I eliminate the hernia on the basis of lack of marked tenderness. Was any history obtained regarding a change in the appearance of this mass in the left groin?

DR. CRYSTAL: There was no change in appearance. She said that it was more tender in the region of the hernia than it had been before the onset.

DR. HAMLIN: That does not help.

I must stick to one thing, and since the apparent gallstone appeals to me, I am going to call this gallstone ileus. I am sure that the surgeon hoped that that was the diagnosis. It is a relatively infrequent condition, and a rather satisfactory one to operate on.

DR. CHESTER M. JONES: Where is the gallstone in gallstone ileus usually found?

DR. HAMLIN: Usually in the lower third of the ileum. Here, it could be close to the terminal ileum. From the story and certain deductions that can be drawn from the films it appears that the major part of the small bowel was affected by the obstruction.

CLINICAL DIAGNOSIS

Gallstone ileus?
Incarcerated femoral hernia?

DR. HAMLIN'S DIAGNOSIS

Gallstone ileus.

ANATOMICAL DIAGNOSIS

Gallstone ileus.

PATHOLOGICAL DISCUSSION

DR. CRYSTAL: We thought that the condition was either a gallstone ileus or an incarcerated hernia. If the former, we considered that operation was contraindicated because of the duration and the patient's age. We did think, however, that it was

worthwhile to subject her to a less serious procedure and gambled on the hernia. She had a hernia, which was incarcerated but not strangulated, with viable omentum. We later operated and found that she had a gallstone of about the expected size. The bowel had no necrosis around it. It was only necessary to make a slit over the stone, deliver it and close the bowel. It was an extremely gratifying operation.

DR. BENJAMIN CASTLEMAN: How far was the tip of the Miller-Abbott tube from the stone?

DR. CRYSTAL: It was within 15 or 20 cm.

DR. HAMLIN: So the stone held tightly.

DR. CRYSTAL: Apparently not, and for that reason we did not use the maneuver of moving the stone back several centimeters rather than cutting into area that had undergone damage. Since the bowel was in good condition there appeared to be no indication for moving the stone.

DR. CASTLEMAN: The operation is a lot easier with the Miller-Abbott tube in place?

DR. HAMLIN: A word might be said about that. In the article that I have previously mentioned, Dr. McKittrick points out that the danger of operation on simple obstruction, without obvious strangulation but with distention of the bowel, is much greater than taking the chance that there may be strangulation and resultant perforation; delay in order to deflate the bowel with a Miller-Abbott tube in obstruction over twenty-four hours old is almost mandatory.

DR. CASTLEMAN: That is the point I wanted to bring out.

Correction. Perusal of the published record of Case 30521, which appeared in the December 28, 1944, issue of the *Journal*, made me suddenly aware of an error in Figure 2, which presented three electrocardiograms taken, respectively, on the day of admission, on the third hospital day and on the fifth hospital day. As had been noted in the protocol of the case and in my own discussion, there was a striking difference between the second electrocardiogram and the first and third tracings. This had, at first, seemed to fit the possibility of a complicating posterior myocardial infarction or a complicating acute cor pulmonale, or both, superimposed on a myocardial infarction that was obvious both by history and electrocardiogram and was evidently anterior in position. There was no posterior myocardial infarction found at autopsy, however, and a possible cor pulmonale resulting from a complete obstruction by an interauricular thrombosis of the right pulmonary veins as they entered the left auricle, and gross infarction of the right lung, should have been apparent at the time of admission, when

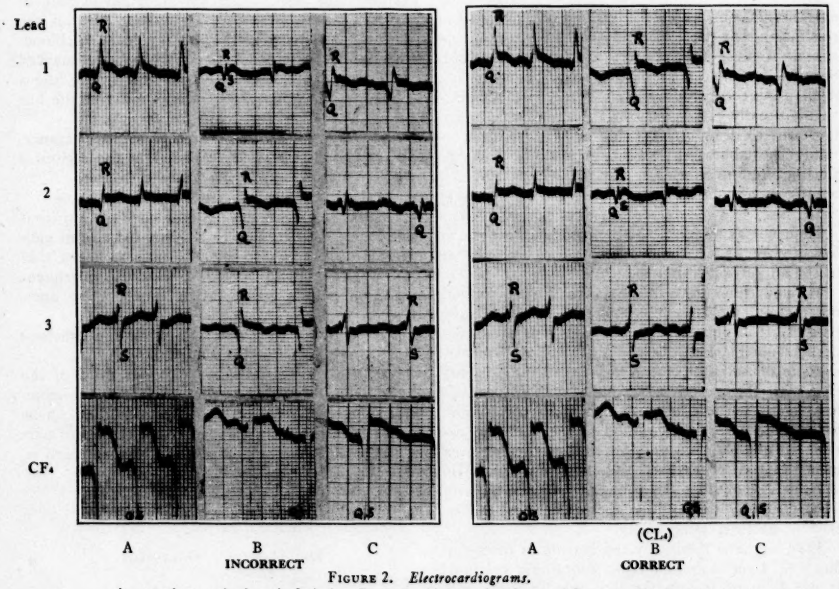

FIGURE 2. *Electrocardiograms.*
A was taken on the day of admission; B, on the third hospital day; and C, on the fifth hospital day.

x-ray evidence of massive involvement of the right lung was already clear. Thus, the confusing change in the electrocardiogram was difficult to explain on the basis of both the clinical and the post-mortem findings.

A closer inspection of the electrocardiographic records revealed at once the probable error that had crept in to cause this confusion. A glance at Figure 2 as published and Figure 2 as corrected, both of which are presented herewith, shows the probability, in fact almost certainty, that in the strip (B) taken on the third hospital day, the original Lead 1 should have been labeled Lead 2, that Lead 2 should have been labeled Lead 1 and that Lead 3 is upside down. This can readily be accounted for by the transposition of the left-arm and left-leg wires, which is less frequent and also more easily overlooked than the error of transposing the arm wires, which results in an inversion of Lead 1, with a switch of Leads 2 and 3. Also, of course, in this record, Lead CF_4 becomes Lead CI_4, since it was the left arm, and not the left leg, that was connected with the chest electrode.

The error in the precordial lead is slight, but that in the limb leads becomes extremely significant. There is no longer a Q wave in Lead 3 and only a small Q wave in Lead 2, whereas the prominent Q wave in Lead 1, also found in the next electrocardiogram, is perfectly consistent with a gross anterior myocardial infarct, as is also the inversion of the T wave in that lead. Although there was no observation at the time of taking this record of the error in the placing of the lead wires, the fact that the electrocardiogram was not taken in the routine work of the Cardiac Laboratory, as well as the confusing picture that resulted and has been explained above, makes it quite certain that an error of technic was responsible for what had seemed like a curious and complicated picture in the electrocardiographic pattern. Thus, the second paragraph of my own discussion of this case, found on page 888, can be completely omitted, with but slight revision of the first paragraph.

Finally, this error and the necessary correction are another example of the constant need of everlasting vigilance in the interpretation of electrocardiograms; one should be particularly on the lookout for the very errors in technic that occurred here. We ourselves have constantly preached about this and yet have here been guilty of the same offense.

PAUL D. WHITE.

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POSTWAR PLANNING

In an editorial carried in the August 31 issue, the *Journal* visualized "a postgraduate medical education program of unprecedented proportions—something that will have to bring into use a larger proportion of clinical material than has ever before been utilized." Under the date of November 9, the Committee on Medical Education and Hospitals of the American Medical Association has addressed a request for information to all hospitals approved for internship and residency, enclosing a copy of a recent report,* in which it was shown that "opportunities for graduate training in surgery, obstetrics-gynecology, otolaryngology and ophthalmology will probably need to be doubled in number while facilities in urology, internal medicine, orthopedics, pediatrics, pathology, radiology, psychiatry and neurology may require an increase of 30 to 70 per cent."

It is conceivable that these increased opportunities may be devised, as and when the war ceases to preoccupy many of the most vigorous and educationally effective members of the profession, thus permitting them to return to peacetime bedsides and operating rooms. Until this is possible, however, it is unrealistic to expect any great expansion of teaching activity. In the request for information referred to above it is stated that training courses in industrial medicine and general medicine will be called for. These are large subjects, having more in common with general practice than they do with the orthodox type of specialty, and they should be made as attractive as possible, since the relative distribution of workers in special and general fields needs sharp adjustment if the people are to be most advantageously served in the future. Up to 1944, for example, more otolaryngologists than internists had been certified and there were nearly as many radiologists as there were surgeons.

In the report, particular attention is called to the fact that there is a major time discrepancy between the courses now available and those that it is estimated will be demanded. Thus, over 90 per cent of the opportunities for postgraduate training in 1943–1944 were in courses of about one month's duration, whereas it is estimated that only 7 per cent of the postwar demand will be for such short courses. How can these longer courses be organized? Here, in prospect, are some thousands of candidates for training — training that will require a greater number of residencies than are now in or readily put into commission on a modern basis. These candidates will tend to compete with one another for the better opportunities, and this competition will, in turn, tend to make of the opportunities themselves a marketable commodity. There is therefore a real need for some sort of supervision by recognized and competent authorities, such as the American Medical Association, the surgeons general of the United States Army, Navy and Public Health Service, the American and the Catholic

*Johnson, V., and Arestad, F. H. Educational facilities required for returning medical officers. *J. A. M. A.* 126:253-257, 1944.

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hospital associations, the American colleges of Surgeons and of Physicians, the boards in the medical specialties, the medical schools, the state licensing boards and medical societies, the Veterans Administration and perhaps many other interested groups. It is good to know that the Massachusetts Medical Society now has a Postwar Planning Committee actively studying the means by which it may be of help in this great task.

DIABETES — A NEGLECTED DISEASE — AND WHAT SHOULD BE DONE ABOUT IT

Diabetes is a neglected disease when compared with tuberculosis or infantile paralysis. Diabetic patients equal in number those with tuberculosis and are four times as numerous as those crippled with infantile paralysis. Yet, contrast the organizations devoted to the control and eradication of tuberculosis throughout the United States and the huge sums raised to combat the disease, as well as the $11,000,000 or more collected for the study and care of cases of infantile paralysis, with the one small national and the four recently created local organizations devoted to diabetes.

The need for an aroused interest in diabetes is growing, because each year the number so afflicted is sure to increase. It is a disease of middle adult life, and the population of the country is steadily advancing to that decade, forty-five to fifty-five years, in which the onset of diabetes is most frequent. Diabetic patients themselves are contributing to the gain in numbers because they are living, on the average, three times as long as they did before the introduction of insulin. Furthermore, increased medical supervision and improved vital statistics are revealing more cases.

Notwithstanding the availability of insulin, many patients still die needlessly of diabetic coma. This could be remedied in a large degree if each hospital in the country would plan and equip itself for the efficient treatment of diabetic emergencies. The time required and the capital involved for equipment would be minimal, and the costs for available services of laboratory personnel at night and on Saturday afternoons, Sundays and holidays would be insignificant compared with that incurred for maintaining operating rooms during those same periods. Indeed, a hospital that does not exercise such foresight in the not distant future may be held derelict to its local needs.

The discovery of alloxan diabetes has opened up opportunities for research never before even dreamed of, and these new pathways of investigation should be exploited. Already, in less than a year and a half following the report of Shaw Dunn's original work, the results of experiments with alloxan have been published from eight different countries.

To treat the rapidly growing number of diabetic patients, to protect them in their emergencies and complications and to foster research, funds are needed, and the most readily available source is from the patients themselves. They constitute an intelligent group and are able and ready to contribute if asked. They are not content with the present methods of treatment. They know that research gave them insulin, and they want to provide for more research to improve present methods of treatment. They are painfully aware of the shortage of hospital beds, not simply for routine care but even for the serious complication of the disease. They appreciate that fellow patients are dying needlessly of diabetic coma because of their lack of a diabetic education or because of inferior medical treatment. They know that diabetes is hereditary, and they wish to protect their families, just as their relatives wish to avoid diabetes. All diabetic patients and their relatives in any community should be asked to furnish the funds for facilities in their local hospital to protect them in emergencies and to promote research in hospitals that are properly qualified. They rightly look on such gifts as personal insurance.

Physicians in the United States should raise $10,000,000 in 1945 for the creation of diabetic funds and for the betterment of hospital facilities. If this is not done, they, too, can be held derelict, because patients and their relatives are more than ready to give the money to improve the care of the diabetic patient.

MASSACHUSETTS MEDICAL SOCIETY

The *Journal* lacks extra copies of the January 13, April 6, May 11, June 1 and July 27, 1944, issues. Many requests have been made by libraries and other subscribers who wish to bind Volumes 230 and 231 but who did not receive those particular issues. If any subscribers who do not bind their copies have the above-mentioned issues on hand, the *Journal* will gladly pay 15 cents for each copy left at or mailed to its office (8 Fenway, Boston 15).

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

DEFIBRINATED HORSE BLOOD FOR LABORATORY USE

For a good many years the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Public Health has been furnishing defibrinated horse blood to various laboratories in the Boston area. As with other products, this has been a free service. In the past, the service has been limited to those who could have the blood picked up by messenger, since no evidence was available that the blood would withstand shipment by mail at all seasons.

Recently there has been an increased demand from hospitals and laboratories in other parts of the Commonwealth for this service. During the past summer a supply of such blood has been mailed to several such laboratories with gratifying results. The blood has arrived in good condition and has obviated the need for bleeding a person or animal for a few red cells every time a batch of culture medium is prepared.

It is now planned to make this service available to all the hospitals and laboratories of the Commonwealth. The requirements are that such institutions return promptly the empty containers for further use and that they gauge their needs so that a minimum of blood will be wasted. Hospitals and laboratories that are placed on the mailing list may receive up to 200 cc. of defibrinated blood at intervals of two weeks. This will ensure a continuous supply of usable blood, since it can be kept in satisfactory condition for this period if properly refrigerated.

Inquiries should be addressed to the Antitoxin and Vaccine Laboratory, 375 South Street, Jamaica Plain 30, attention of Dr. J. A. McComb.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Textbook of Gynecology. By Emil Novak, M.D., associate in gynecology, Johns Hopkins University School of Medicine, and gynecologist, Bon Secours and St. Agnes hospitals, Baltimore. Second edition. 8°, cloth, 708 pp., with 456 illustrations. Baltimore: William and Wilkins Company, 1944. $8.00.

This second edition of a textbook first published in 1941 has been thoroughly revised and brought up to date, which necessitated a complete resetting of the text. Many new original illustrations, including a considerable group of color photographs, have been added. Two new chapters, covering the embryology of the female generative organs and the female urologic conditions that are of special interest to the gynecologist, are included. The work has been written primarily for students and general practitioners, and for this reason details of operative technic have been omitted.

An Introduction to Public Health. By Harry S. Mustard, M.D., LL.D., director and professor of public health practice, Delamar Institute of Public Health, College of Physicians and Surgeons, Columbia University, New York City. Second edition. 8°, cloth, 283 pp. New York: Macmillan Company, 1944. $3.25.

The first edition of this manual was written in 1935, and this new edition has been completely revised and brought into conformity with modern practice in the public-health field. Two chapters, one on industrial hygiene and the other on medical care, have been added, and the morbidity and mortality data reflect the latest available statistics. The volume is designed for use in all introductory courses in public health whether in schools of public health, in medical schools, in nursing schools or in colleges.

Our Concern — Every Child: State and community planning for wartime and postwar security of children. By Emma O. Lundberg. Children's Bureau, Publication 303. 8°, paper, 84 pp. Washington: Government Printing Office, 1944. 15 cents.

This pamphlet discusses in an abbreviated form the welfare of children in peace and in war from the viewpoints of both the state and the community. It provides outlines for planning services in all their aspects for the welfare of children.

Malaria: Its diagnosis, treatment and prophylaxis. By William N. Bispham, M.D. 8°, cloth, 197 pp., with 4 plates and frontispiece. Baltimore: Williams and Wilkins Company, 1944. $3.50.

This small book has been written to give the physician a knowledge of the clinical features of malaria. It considers etiology, symptomatology, diagnosis, pathology, treatment, prevention and immunity. Blackwater fever is briefly discussed. The final chapter is on prevention and treatment of malaria in West Africa and is contributed by Dr. L. T. Coggeshall. The first two chapters comprise a short history of malaria and its geographic distribution. A good index makes all material available, and this manual should be useful as a reference source.

Plaster of Paris Technic. By Edwin O. Geckeler, M.D., associate professor of orthopedic surgery and chief of the Fracture Service, Hahnemann Medical College and Hospital, Philadelphia. 8°, cloth, 220 pp., with 208 illustrations. Baltimore: Williams and Wilkins Company, 1944. $3.00.

Unusually well illustrated and suitable for the instruction of graduate and undergraduate students, the text gives a

practical working knowledge of the everyday conditions in which plaster of Paris may be used. There are special chapters on its use in war surgery and in the treatment of burns.

Strophanthin: Clinical and experimental experiences of the past twenty-five years. By Bruno Kisch, M.D. 8°, cloth, 158 pp., with 24 illustrations. New York: Brooklyn Medical Press, 1944. $4.00.

This monograph has been written for the purpose of urging the American medical profession to reconsider the question of the clinical application of strophanthin. In his text the author embodies conclusions derived from a number of experiments on animals and records his clinical observations, particularly those on how the drug affects the vagus nerve and on how the extrasystoles should be judged after strophanthin administration. A comprehensive review of the literature of the past twenty-five years has been appended to the text. The book is well printed, with a good type on good paper.

The Blood Pressure and Its Disorders including Angina Pectoris. By John Plesch, M.D. (Budapest), M.D. (Berlin), L.R.C.P. and S. (Edin. and Glas.). 8°, cloth, 149 pp., with 61 illustrations. Baltimore: Williams and Wilkins Company, 1944. $4.50.

This small manual discusses arterial and venous blood pressures, with particular reference to angina pectoris.

Fertility in Women: Causes, diagnosis and treatment of impaired fertility. By Samuel L. Siegler, M.D., attending obstetrician and gynecologist, Brooklyn Women's Hospital, attending gynecologist, Unity Hospital, assistant obstetrician and gynecologist, Greenpoint Hospital, and consultant in gynecology, Rockaway Beach Hospital. With a foreword by Robert L. Dickinson, M.D. 8°, cloth, 450 pp., with 194 illustrations. Philadelphia: J. B. Lippincott Company, 1944. $4.50.

The various aspects of abnormal and impaired fertility are discussed from a systemic or functional point of view. There is a long chapter on the physiology of the female sex cycle and the various methods for evaluating its efficiency. Considerable space is devoted to both general and specific therapy, to the treatment of ovarian imbalance and to the faulty reception of spermatozoa.

Manual of Psychological Medicine for Practitioners and Students. By A. F. Tredgold, M.D., F.R.C.P., F.R.S.E., consulting physician, University College Hospital, London, and lecturer on mental deficiency, London University. 8°, cloth, 298 pp. Baltimore: Williams and Wilkins Company, 1943. $5.00.

This small book is essentially a manual on disorders of the mind for the use of all those who are brought into contact with military personnel.

The Diseases of the Endocrine Glands. By Herman Zondek, M.D. (Berlin), director of the Medical Division, Bikur Cholim Hospital, Jerusalem. Translated by Carl Prausnitz Giles, M.D. (Breslau), M.R.C.S. (Eng.), L.R.C.P. (Lond.). Fourth (second English) edition. 8°, cloth, 496 pp., with 180 illustrations. Baltimore: Williams and Wilkins Company, 1944. $11.00.

The first edition of this book was written in 1935, and the present edition has been revised to embody important results of recent researches.

Manual of Military Neuropsychiatry. Edited by Harry C. Solomon, M.D., professor of psychiatry, Harvard Medical School, and medical director, Boston Psychopathic Hospital; and Paul I. Yakovlev, M.D., clinical director, Walter E. Fernald State School, and instructor of neurology, Harvard Medical School. 12°, cloth, 746 pp., with 15 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. $6.00.

This manual is intended as a reference text on topics of clinical neurology and psychiatry and has been prepared especially for medical officers, often remote from libraries and textbooks. The book is divided into six parts: history of neuropsychiatry during World War I and general organization during the current war; induction (having to do with the screening and examination of inductees); administration and disposition; clinical entities; prophylaxis and therapy; and special topics.

Secretory Mechanism of the Digestive Glands. By B. P. Babkin, M.D., D.Sc., LL.D., research professor of physiology, McGill University, Montreal. 8°, cloth, 900 pp., with 220 illustrations. New York: Paul B. Hoeber, Incorporated, 1944. $12.75.

This new book on the physiology of the digestive glands embodies the work performed by the author and his coworkers during the last fourteen years in the Department of Physiology of McGill University. It is not monographic in scope, since no attempt has been made to review the whole of the literature concerned with the secretory function of all the digestive glands. The book deals mainly with the mechanisms regulating secretory activity, as exemplified in particular by the functions of the gastric, salivary and pancreatic glands. So far as possible, the author has included in his work the more important facts known in regard to the secretory functions of the digestive tracts up to the present date. An extensive bibliography is appended to the text.

The Radiology of Bones and Joints. By James F. Brailsford, M.D., Ph.D., F.R.C.P., F.I.C.S., Hunterian professor, Royal College of Surgeons, England (1934–1935 and 1943–1944), radiological demonstrator in living anatomy, University of Birmingham, radiologist to St. Chad's Hospital, the City of Birmingham Infant Welfare Centres and the Military Hospital, Hollymoor, Birmingham, and consulting radiologist to the City of Birmingham Hospitals, the Robert Jones and Agnes Hunt Orthopaedic Hospital, the Birmingham Accident Hospital and Rehabilitation Centre and the Birmingham Mental Hospital. Third edition. 8°, cloth, 440 pp., with 404 illustrations. Baltimore: Williams and Wilkins Company, 1944. $12.00.

Ten years have elapsed since the publication of the second edition of this special work, first published in 1934. The book now represents an analysis of the work of the author during the past twenty-five years. The present edition gives a more comprehensive account of the variations of the normal developmental and the pathologic conditions in bones and joints than was possible in the earlier editions. Particular attention has been paid to the changes in bones and joints resulting from trauma, the osseous dystrophies, tuberculosis, syphilis and neoplasms. The treatment of certain conditions has been considered in the light of radiographic findings. An extensive bibliography is appended to the text. The type and paper are good, and there are many full-page radiographic plates.

Diseases of the Digestive System. Edited by Sidney A. Portis, M.D., associate professor of medicine, University of Illinois (Rush) Medical School, attending physician, Michael Reese Hospital, consulting physician, Cook County Hospital, and

consultant in medicine, Institute of Psychoanalysis, Chicago. 8°, cloth, 932 pp., with 182 illustrations. Philadelphia: Lea and Febiger, 1944. $11.00.

This second edition of an authoritative work by fifty contributors has been completely revised and reorganized to meet the needs of students and teachers in the field. Special emphasis has been placed on the psychosomatic aspects of gastrointestinal symptoms. The chapters have been rearranged, placing the physiology of each organ before its clinical discussion. Each contributor has considered the effects of emotional stimuli on the gastrointestinal tract. The chapter on psychosomatic disturbances has been enlarged. Selected references have been appended to each chapter.

Recent Advances in Anaesthesia and Analgesia, including Oxygen Therapy. By C. Langdon Hewer, M.B., B.S. (Lond.), D.A. (Eng.), senior anaesthetist, St. Bartholomew's Hospital and St. Andrew's Hospital, Dollis Hill, anaesthetist, Brompton Chest Hospital and Emergency Medical Service, and consulting anaesthetist, Mid-Herts and West-Herts hospitals. Fifth edition. 8°, cloth, 343 pp., with 141 illustrations. Philadelphia: Blakiston Company, 1944. $5.50.

In this edition it has been possible to include new material on a large number of important subjects. Each section has been carefully revised throughout, and attention has been given to the military aspects of anesthesia. An additional chapter on anesthetic charts and records has been placed at the end of the book. To each chapter has been appended a selected list of references.

The Urinary Tract: A handbook of roentgen diagnosis. By H. Dabney Kerr, M.D., professor of radiology, State University of Iowa College of Medicine; and Carl L. Gillies, M.D., associate professor of radiology, State University of Iowa College of Medicine. 8°, cloth, 320 pp., with 120 illustrations. Chicago: Year Book Publishers, Incorporated, 1944. $5.50.

The objective of this small handbook is to provide student, practitioner, urologist and radiologist with selected plates of the commoner and some of the uncommon lesions of the urinary tract. The plates are of cases studied radiographically at the University of Iowa hospitals. All reproductions show the structures at about a third of the actual size, and no retouching has been done on the negatives. In every case illustrating pathologic involvement, the hospital record of the patient has been examined and the diagnosis has been based to a large extent on the study of all available information. Whenever possible, several examples of each condition have been included, because of the fact that no two normal structures or no two lesions appear exactly alike. The text is divided arbitrarily into sections on the kidneys, ureter, bladder and urethra.

Freud's Contribution to Psychiatry. By A. A. Brill, Ph.B., M.D. 12°, cloth, 244 pp. New York: W. W. Norton and Company, Incorporated, 1944. $2.75.

The author presents an intimate evaluation of the development of psychoanalysis as he himself lived through it, emphasizing the statements with appropriate quotations from his extensive correspondence with Freud. Dr. Brill was one of the pioneers of psychoanalysis and since 1907 has devoted all his time to the study and dissemination of Freud's teachings. He was Freud's first English translator, his most active expositor in this country and his most ardent co-worker and close friend.

Foster Home Care for Mental Patients. By Hester B. Crutcher, director of social work, State of New York Department of Mental Hygiene. 8°, cloth, 199 pp. New York: The Commonwealth Fund, 1944. $2.00.

The author discusses the meaning and the objectives of family care, its development in the United States and foreign countries, some of the results achieved, the financial as well as the therapeutic advantages, various procedures, including selection and supervision of cases, and forms for keeping the necessary records. Foster-family care is care under hospital supervision of mentally ill persons or mental defectives in families other than their own. It is not mere custody but therapeutic care under the supervision of the mental hospital. It is a recent development in the United States.

The Medical Clinics of North America. Boston Number: September, 1944. 8°, cloth, 263 pp., illustrated. Philadelphia: W. B. Saunders Company, 1944. $3.00.

NOTICES

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, March 1, in the classroom of the Nurses' Residence at 7:15 p.m. The topic will be "Selection of Hypertensive Patient for Sympathectomy." Dr. Dera Kinsey will be chairman.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday, March 2 — The Significance of the Eosinophil Count in Acute Infections. Dr. Francis C. Lowell.

Wednesday, March 7 — Dental Medicine. Dr. Robert W. Buck.

Friday, March 9 — Protein Nutrition in Problems of Medical Interest. Dr. Fredrick J. Stare.

Wednesday, March 14 — The Glaucoma Problem and General Medicine. Dr. Joseph Igersheimer.

Friday, March 16 — Protolytic Enzymes in Tissues. Dr. Paul C. Zamecnik.

Wednesday, March 21 — The Diagnosis of Diabetes Mellitus. Dr. Joseph Rosenthal.

Friday, March 23 — Some Aspects of Cardiac Surgery. Dr. Robert E. Gross.

Wednesday, March 28 — The Surgical Gallbladder. Dr. Leland S. McKittrick.

Friday, March 30 — Graphic Methods and Auscultation of the Heart. Dr. Aldo A. Luisada.

On Monday mornings (except March 12) clinics will be given by Dr. Samuel Proger. On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings clinics will be given by Dr. William Dameshek.

(*Notices continued on page xvii*)